Appendix A: List of Acronyms

%	percent
ACE	angiotensin-converting-enzyme
ACS	acute coronary syndrome
ACT	Acetylcysteine for Contrat-Induced Nephropathy Trial
AHRQ	Agency for Healthcare Research and Quality
AKI	Acute kidney injury
ALT	alanine aminotransferase
AMI	acute myocardial infarction
ARB	angiotensin II receptor blockers
CHF	congestive heart failure
CI	Confidence interval
CIN	Contrast induced nephropathy
CKD	Chronic Kidney disease
CM	Contrast media
Cr	Creatinine
CrCl	Creatinine clearance
CT	Computed tomography
eGFR	estimated glomerular filtration rate
EPC	Evidence-based practice center
ESRD	end stage renal disease
GFR	Glomular filtration rate
HD	hemodialysis
HF	hemofiltration
HOCM	high osmolar contrast media
ICU	intensive care unit
IOCM	Iso-osmolar contrast media
KQ	Key Question
LOCM	Low-osmolar contrast media
LVEF	Left Ventricular Ejection Fraction
MACE	Major adverse cardiac events
MeSH	Medical subject heading
MI	myocardial infarction
NAC	n-acetylcyateine
NaCL	Sodium chloride
NaHCO3	Sodium bicarbonate
NR	Not reported
NS	Not significant
OR	odds ratio
PCI	percutaneous coronary intervention
PICOTS	Populations, interventions, comparators, outcomes, timing, setting
RCT	Randomized controlled trial
RR	Relative risk
RRT	Renal replacement therapy
SD	Standard deviation
SrCr	Serum creatinine
STEMI	ST Elevation Myocardial Infarction
T2DM	Type 2 diabetes mellitus
TOO	Task Order Officer

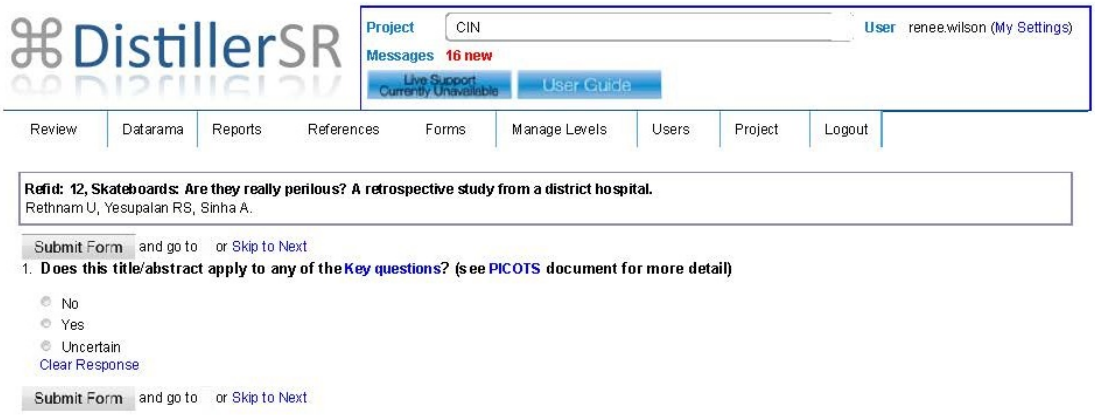
Appendix B. Detailed Search Strategy

Database	Search	Included returns	Notes
PubMed	(("Kidney diseases"[mh] OR "Kidney disease"[tiab] OR "kidney diseases"[tiab] OR Nephropathy[tiab] OR "acute kidney injury"[mh] OR "acute kidney injury"[tiab] OR “acute renal injury”[tiab] OR "renal disease"[tiab] OR “renal diseases”[tiab]) AND ("contrast media"[mh] OR "contrast media"[tiab] OR "contrast medium"[tiab] OR "contrast material"[tiab])) NOT (animal[mh] NOT human[mh])	5308	
Embase	('contrast medium'/exp OR 'contrast medium':ab,ti OR 'contrast media':ab,ti OR 'contrast material':ab,ti) AND ('kidney disease'/exp OR 'kidney disease':ab,ti OR 'kidney diseases':ab,ti OR nephropathy:ab,ti OR 'acute kidney injury':ab,ti OR 'renal disease':ab,ti OR 'acute renal failure':ab,ti OR 'acute renal injury':ab,ti)	8952	12151 Limit to humans (study type): 9972 Limit to Article, Review, Conference Abstract, Conference Paper, Short Survey, Article in Press, Conference review (Publication type): 8952
Cochrane	ID Search #1 MeSH descriptor: [Kidney Diseases] explode all trees #2 "kidney disease":ti,ab,kw (Word variations have been searched) #3 nephropathy:ti,ab,kw (Word variations have been searched) #4 "acute kidney injury":ti,ab,kw (Word variations have been searched) #5 "renal disease":ti,ab,kw (Word variations have been searched) #6 "acute renal injury":ti,ab,kw #7 "renal diseases":ti,ab,kw #8 #1 or #2 or #3 or #4 or #5 or #6 or #7 #9 MeSH descriptor: [Contrast Media] explode all trees #10 "contrast media":ti,ab,kw (Word variations have been searched) #11 "contrast material":ti,ab,kw (Word variations have been searched) #12 "contrast medium":ti,ab,kw #13 #9 or #10 or #11 or #12 #14 #8 and #13	429	Other reviews: 52 Trials: 368 Technology assessments: 4 Economic evaluations: 5
Total		14,689	

Appendix C: Screening and Data Abstraction Forms

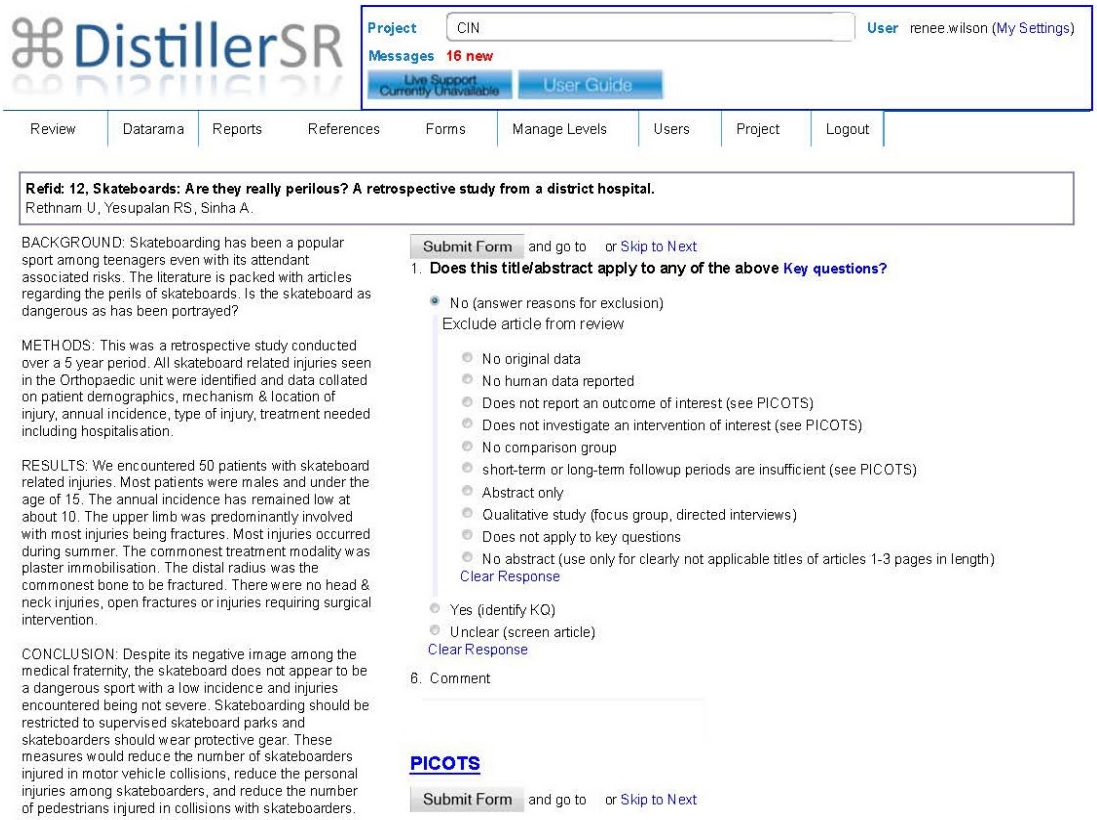
Title

DistillerSR https://systematic-review.ca/Submit/RenderForm.php?id=1&hide_abstract=1

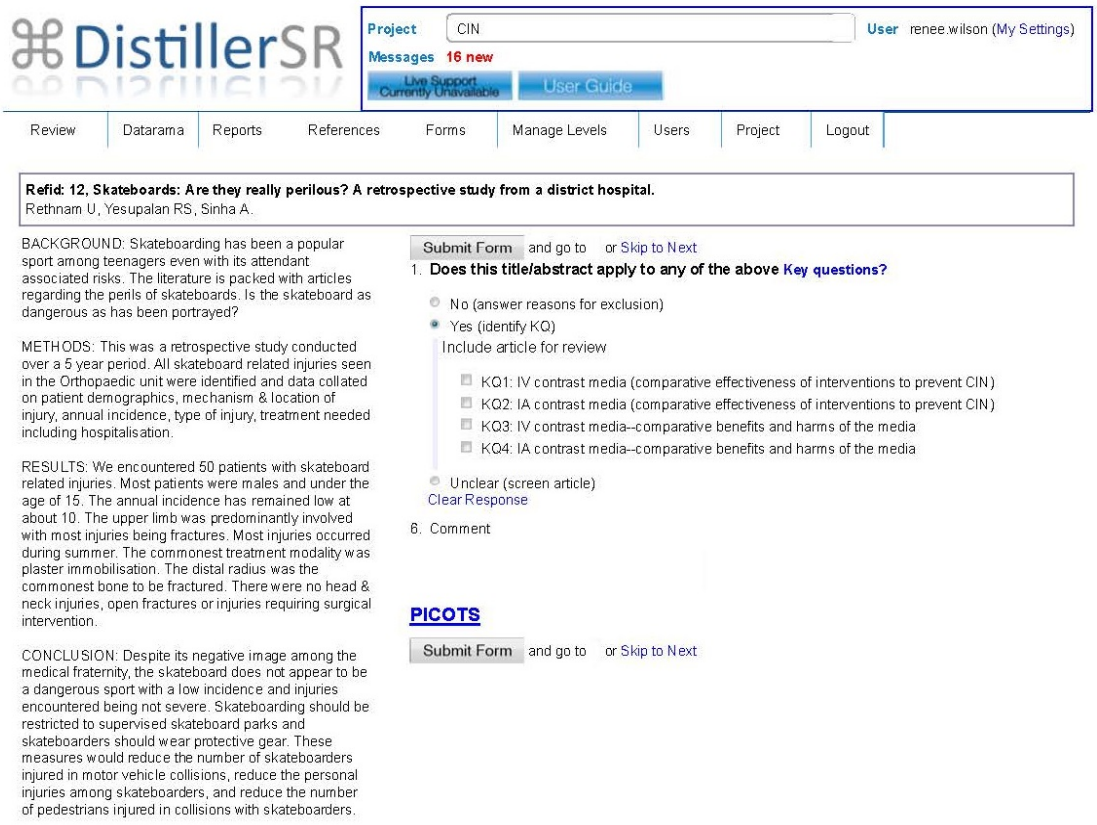


Abstract Screening– NO

DistillerSR https://systematic-review.ca/Submit/RenderForm.php?id=4

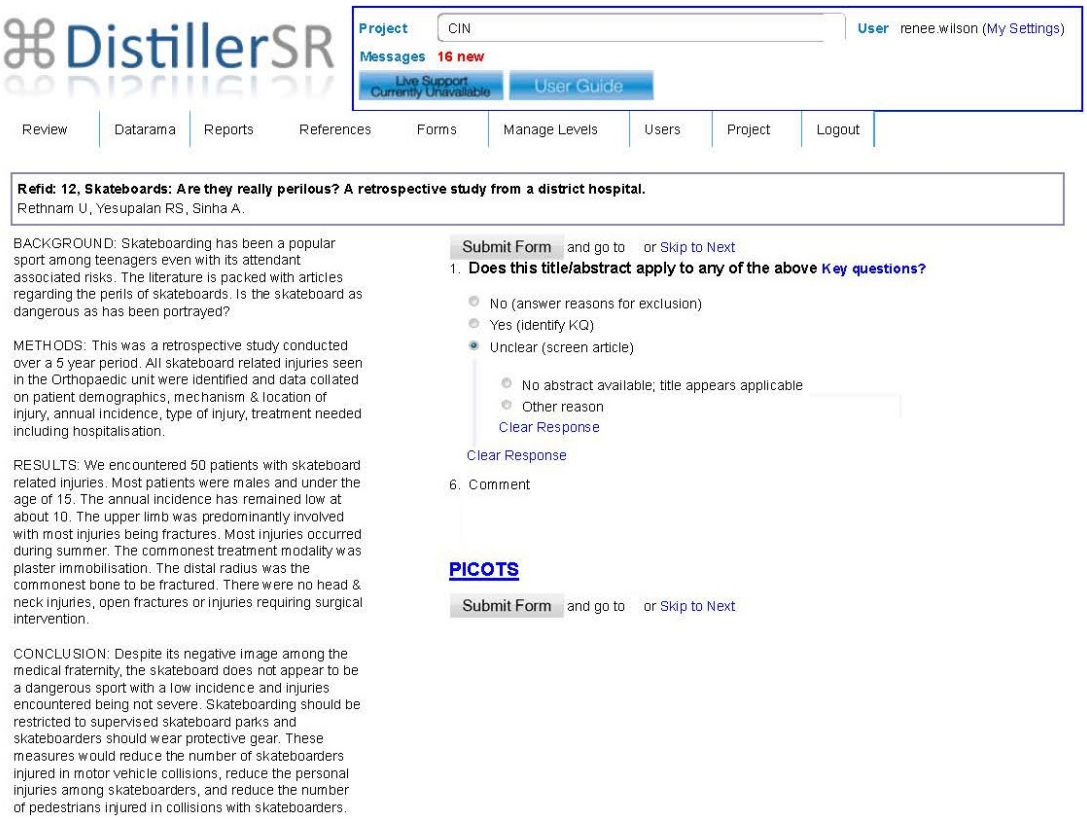


Abstract Screening– YES

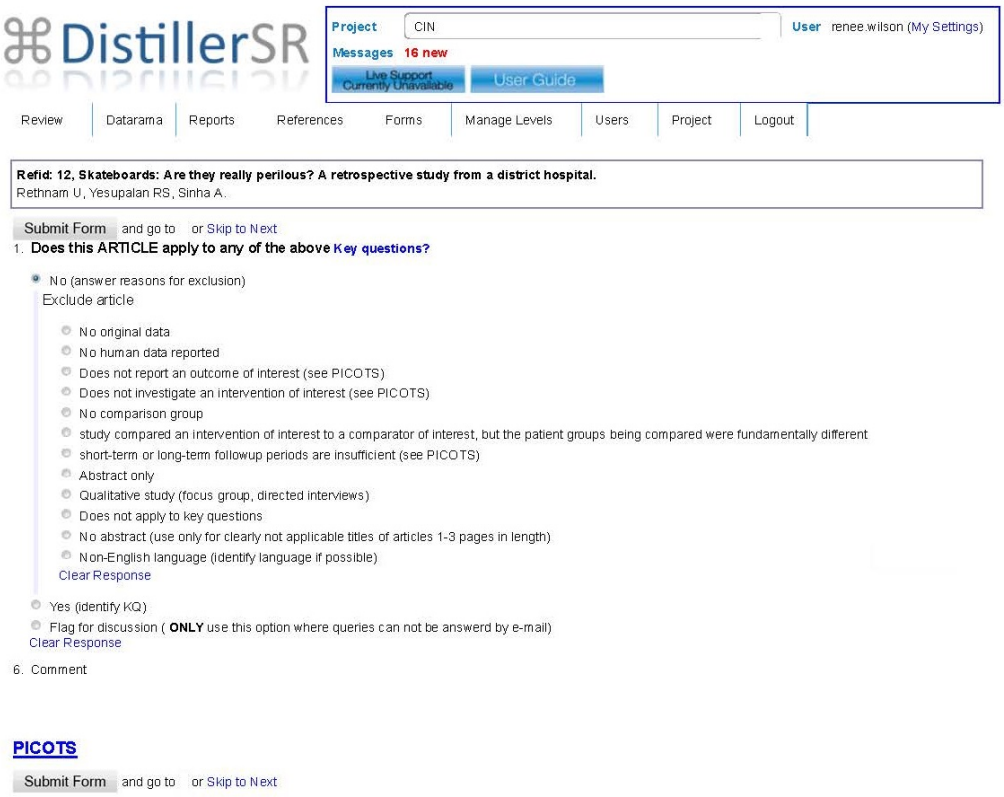


Abstract Screening– Unclear

DistillerSR https://systematic-review.ca/Submit/RenderForm.php?id=4

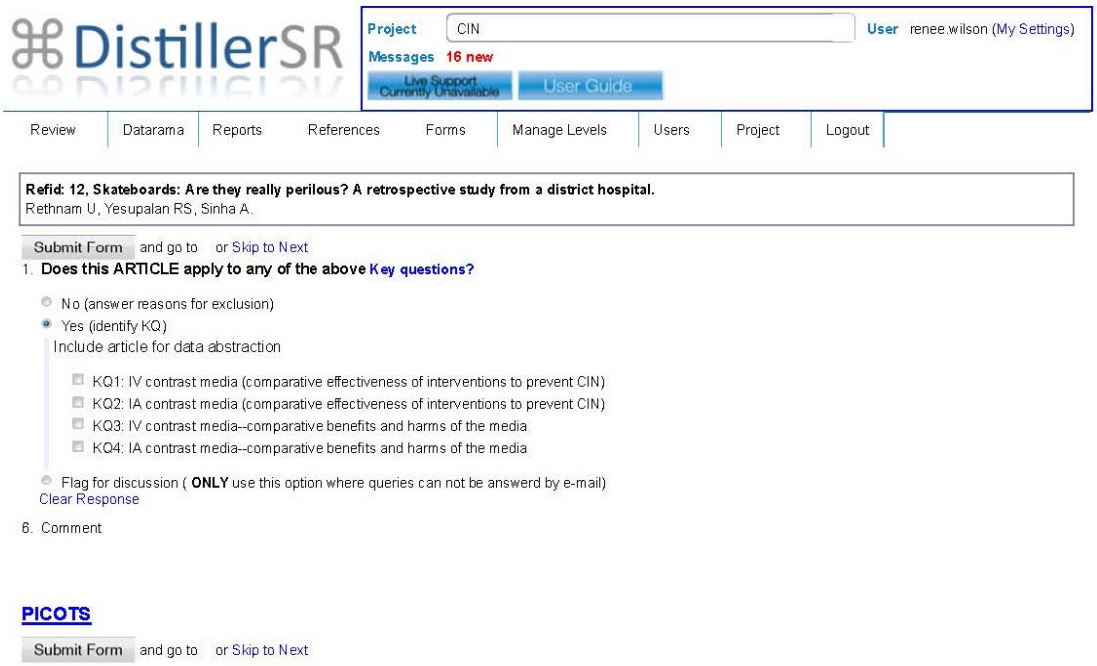


Article Screening– NO



Article Screening– YES

DistillerSR https://systematic-review.ca/Submit/RenderForm.php?id=6&hide_abstract=1



Participant Characteristics

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Rethnam U, Yesupalan RS, Sinha A.

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Participant Characteristics at Baseline

1. Does the study report baseline characteristics for subgroups seperately?
(e.g., IV administration and IA administration)

- (•) Yes
- ( ) No

Clear Response

2. Identify group for baseline characteristics
(You can submit this form multiple time)

Select an Answer

Arm 1 (control/usual care)	Arm 2	Arm 3	Arm 4	Arm 5
3.	4.	5.	6.	7.

8. N at baseline

- [ ] Total N
- [ ] Arm 1 (control/usual care) n
- [ ] Arm 2
- [ ] Arm 3
- [ ] Arm 4
- [ ] Arm 5
- [ ] Not reported

	Follow-up	Mean, median, max/min...	Units
9. ( ) Not reported Clear Response	10.	11. Select an Answer	12. Select an Answer

13. Sex

- (•) reported

Overall Group	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5

14.	15.	16.	17.	18.	19.
☐ women, n ☐ women, %	☐ women, n ☐ women, %	☐ women, n ☐ women, %	☐ women, n ☐ women, %	☐ women, n ☐ women, %	☐ women, n ☐ women, %

○ not reported

20. Age

◉ reported

Overall Group	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
21. ☐ mean ☐ Median ☐ Range	22. ☐ mean ☐ Median ☐ Range	23. ☐ mean ☐ Median ☐ Range	24. ☐ mean ☐ Median ☐ Range	25. ☐ mean ☐ median ☐ range	26. ☐ mean ☐ median ☐ range

○ not reported

27. Race/ethnicity

◉ Reported

	Overall Group	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
White, non-Hispanic	28. ☐ n ☐ %	29. ☐ n ☐ %	30. ☐ n ☐ %	31. ☐ n ☐ %	32. ☐ n ☐ %	33. ☐ n ☐ %
Black, non-Hispanic	34. ☐ n ☐ %	35. ☐ n ☐ %	36. ☐ n ☐ %	37. ☐ n ☐ %	38. ☐ n ☐ %	39. ☐ n ☐ %
Latino/Hispanic	40. ☐ n ☐ %	41. ☐ n ☐ %	42. ☐ n ☐ %	43. ☐ n ☐ %	44. ☐ n ☐ %	45. ☐ n ☐ %
Asian/Pacific Islander	46. ☐ n ☐ %	47. ☐ n ☐ %	48. ☐ n ☐ %	49. ☐ n ☐ %	50. ☐ n ☐ %	51. ☐ n ☐ %
American Indian/Alaska Native	52. ☐ n ☐ %	53. ☐ n ☐ %	54. ☐ n ☐ %	55. ☐ n ☐ %	56. ☐ n ☐ %	57. ☐ n ☐ %
58. Other	59. ☐ n ☐ %	60. ☐ n ☐ %	61. ☐ n ☐ %	62. ☐ n ☐ %	63. ☐ n ☐ %	64. ☐ n ☐ %

65. Other	66. n %	67. n %	68. n %	69. n %	70. n %	71. n %
72. Other	73. n %	74. n %	75. n %	76. n %	77. 2n %	78. 2n %

○ not reported

79. Education

◉ Reported

	Overall Group	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
< High School	80. n %	81. n %	82. n %	83. n %	84. n %	85. n %
Completed High School	86. n %	87. n %	88. n %	89. n %	90. n %	91. n %
College Degree	92. n %	93. n %	94. n %	95. n %	96. n %	97. n %
Post-graduate Degree	98. n %	99. n %	100. n %	101. n %	102. n %	103. n %
Years of education	104. mean median min max	105. mean median min max	106. mean median min max	107. mean median min max	108. mean median min max	109. mean median min max
110. Other	111. n %	112. n %	113. n %	114. n %	115. n %	116. n %
117. Other	118. n %	119. n %	120. n %	121. n %	122. n %	123. n %

124. Other	125. ☐ n ☐ %	126. ☐ n ☐ %	127. ☐ n ☐ %	128. ☐ n ☐ %	129. ☐ n ☐ %	130. ☐ n ☐ %

○ not reported

131. Smoking

◉ reported

	Overall Group	Arm 1	Arm 2	Arm 3	Arm 4	Arm 5
Current	132. ☐ n ☐ %	133. ☐ n ☐ %	134. ☐ n ☐ %	135. ☐ n ☐ %	136. ☐ n ☐ %	137. ☐ n ☐ %
Former	138. ☐ n ☐ %	139. ☐ n ☐ %	140. ☐ n ☐ %	141. ☐ n ☐ %	142. ☐ n ☐ %	143. ☐ n ☐ %
Ever	144. ☐ n ☐ %	145. ☐ n ☐ %	146. ☐ n ☐ %	147. ☐ n ☐ %	148. ☐ n ☐ %	149. ☐ n ☐ %
Never	150. ☐ n ☐ %	151. ☐ n ☐ %	152. ☐ n ☐ %	153. ☐ n ☐ %	154. ☐ n ☐ %	155. ☐ n ☐ %

○ not reported

156. Is the entire study population a subgroup (all particiupants have a specific disease or condition)?

◉ Yes

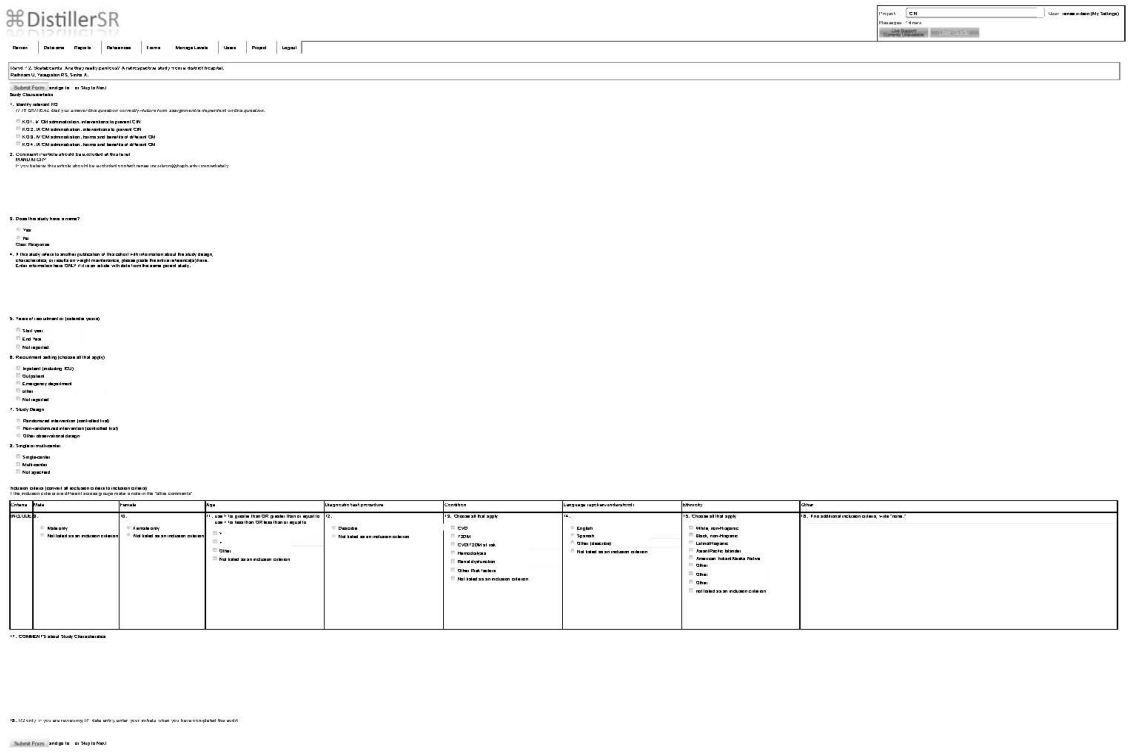
Condition	Define
Renal insufficiency (included CKD)	157.
Diabetes	158.
On Dialysis	159.
160. Other	161.
162. Other	163.

166. Other Comments

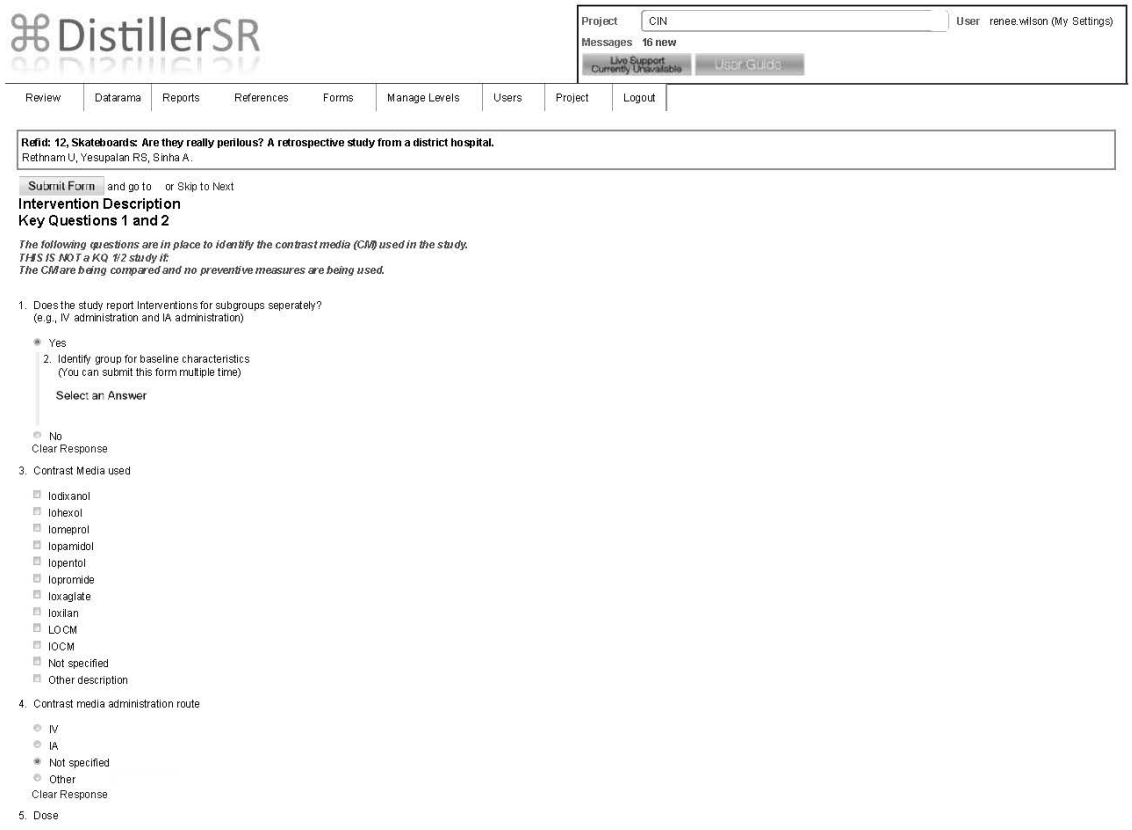
167. **R2 only: if you are reviewing R1 data entry, enter your initials when you have completed the audit**

Submit Form and go to or Skip to Next

Study Characteristics



Intervention KQ 1&2



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Refid: 12, Skateboards: Are they really perilous? A retrospective study from a district hospital.
Rethnam U, Yesupalan RS, Sinha A.

Submit Form and go to or Skip to Next

Intervention Description
Key Questions 1 and 2

The following questions are in place to identify the contrast media (CM) used in the study.
THIS IS NOT a KQ 1/2 study if:
The CM are being compared and no preventive measures are being used.

1. Does the study report interventions for subgroups seperately?
(e.g., IV administration and IA administration)

- (•) Yes
  2. Identify group for baseline characteristics
  (You can submit this form multiple time)
  Select an Answer
- ( ) No

Clear Response

3. Contrast Media used

- [ ] Iodixanol
- [ ] Iohexol
- [ ] Iomeprol
- [ ] Iopamidol
- [ ] Iopentol
- [ ] Iopromide
- [ ] Ioxaglate
- [ ] Ioxilan
- [ ] LOCM
- [ ] IOCM
- [ ] Not specified
- [ ] Other description

4. Contrast media administration route

- ( ) IV
- ( ) IA
- (•) Not specified
- ( ) Other

Clear Response

5. Dose

- Define
- Not specified

6. Duration

- Define
- Not specified

Clear Response

7. Volume

- Define
- Not specified

Clear Response

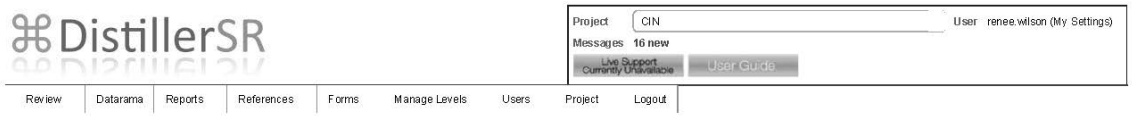
The following questions are in place to idnetify and describe preventive measures for CIN.
Use Arm 1 EXCLUSIVELY for the control or standard care intervention. If there is not control, leave those columns blank under Arm 1
NOTE: the Arms below should match teh Arms described in the participant characteristics form.

	Arm 1 (control/usual care)	Arm 2	Arm 3	Arm 4	Arm 5
Administration route	8. **NO CONTROL OR USUAL CARE** Oral IV Not reported Other	9. Oral IV Not reported Other	10. Oral IV Not reported Other	11. Oral IV Not reported Other	12. Oral IV Not reported Other
Dose	13.	14.	15.	16.	17.
Duration	18.	19.	20.	21.	22.
Temporal association to CM administration	23. Prior to CM admin During CM admin After CM admin Not stated Other	24. Prior to CM admin During CM admin After CM admin Not stated Other	25. Prior to CM admin During CM admin After CM admin Not stated Other	26. Prior to CM admin During CM admin After CM admin Not stated Other	27. Prior to CM admin During CM admin After CM admin Not stated Other
Other details	28.	29.	30.	31.	32.

33. Comments

34. **R2 only: if you are reviewing R1 data entry, enter your initials when you have completed the audit**

Intervention KQ 3&4



Refid: 12, Skateboards: Are they really perilous? A retrospective study from a district hospital.
Rethnam U, Yesupalan RS, Sinha A.

Submit Form and go to or Skip to Next

Intervention Description
Key Questions 3_4

The following questions are in place to identify and describe contrast media (CM) only.
Use Arm 1 EXCLUSIVELY for the control or standard care intervention. If there is no control, leave those columns blank under Arm 1
NOTE: the Arms below should match the Arms described in the participant characteristics form.

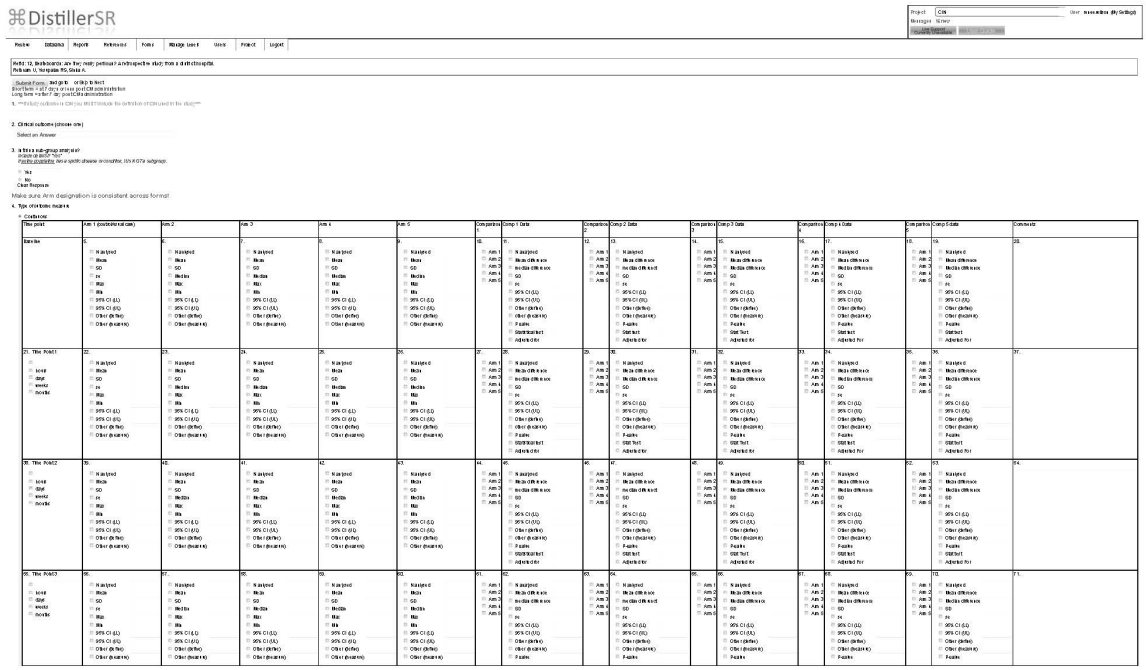
1. Does the study report Interventions for subgroups seperately?
(e.g., IV administration and IA administration)

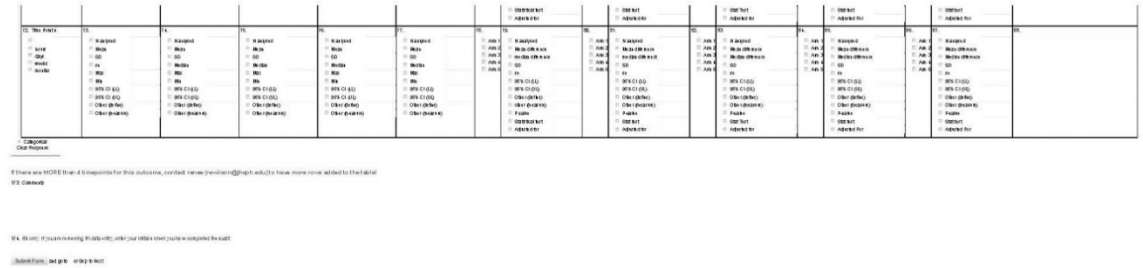
- (•) Yes
  2. Identify group for baseline characteristics
  (You can submit this form multiple time)
  Select an Answer
- ( ) No

Clear Response

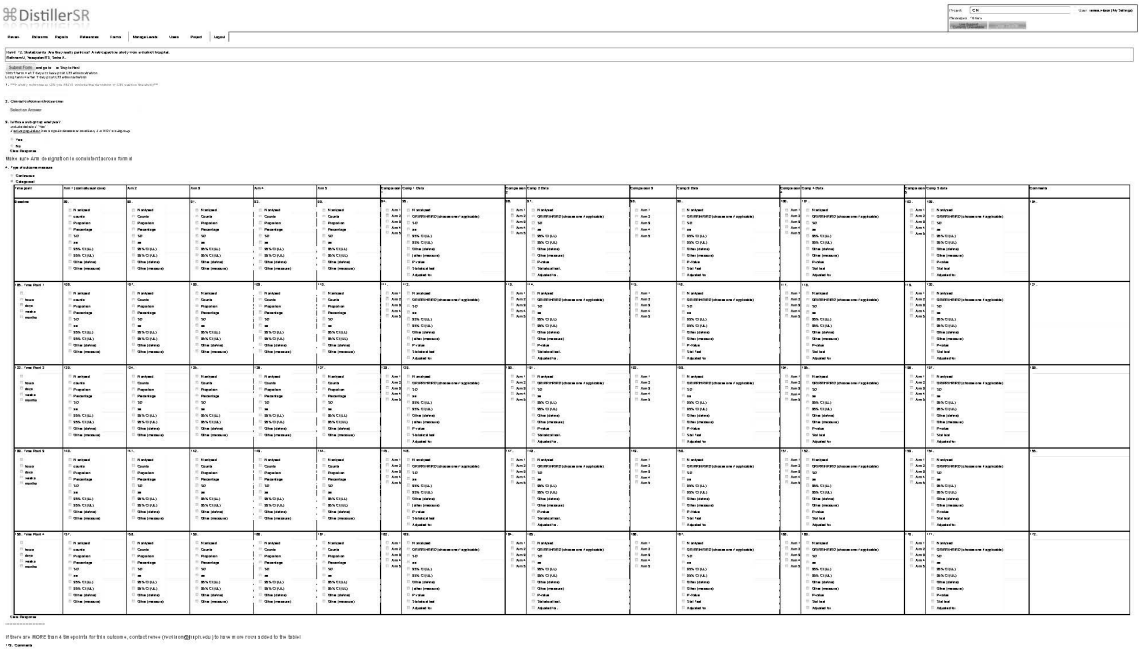
	Arm 1 (control/usual care)	Arm 2	Arm 3	Arm 4	Arm 5
Contrast Medium (Media) used	3. ☐ Iodixanol ☐ Iohexol ☐ Iomeprol ☐ Iopamidol ☐ Iopentol ☐ Iopromide ☐ Ioxaglate ☐ Ioxilan ☐ LOCM ☐ IOCM ☐ Not specified ☐ Other description	4. ☐ Iodixanol ☐ Iohexol ☐ Iomeprol ☐ Iopamidol ☐ Iopentol ☐ Iopromide ☐ Ioxaglate ☐ Ioxilan ☐ LOCM ☐ IOCM ☐ Not specified ☐ Other description	5. ☐ Iodixanol ☐ Iohexol ☐ Iomeprol ☐ Iopamidol ☐ Iopentol ☐ Iopromide ☐ Ioxaglate ☐ Ioxilan ☐ LOCM ☐ IOCM ☐ Not specified ☐ Other description	6. ☐ Iodixanol ☐ Iohexol ☐ Iomeprol ☐ Iopamidol ☐ Iopentol ☐ Iopromide ☐ Ioxaglate ☐ Ioxilan ☐ LOCM ☐ IOCM ☐ Not specified ☐ Other description	7. ☐ Iodixanol ☐ Iohexol ☐ Iomeprol ☐ Iopamidol ☐ Iopentol ☐ Iopromide ☐ Ioxaglate ☐ Ioxilan ☐ LOCM ☐ IOCM ☐ Not specified ☐ Other description
Administration route	8. ☐ **NO CONTROL OR USUAL CARE** ☐ IV ☐ IA ☐ Not reported ☐ Other	9. ☐ IV ☐ IA ☐ Not reported ☐ Other	10. ☐ IV ☐ IA ☐ Not reported ☐ Other	11. ☐ IV ☐ IA ☐ Not reported ☐ Other	12. ☐ IV ☐ IA ☐ Not reported ☐ Other

Clinical Outcomes Continuous





Clinical Outcomes Categorical



Adverse Events

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Rethnam U, Yesupalan RS, Sinha A.

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Adverse events

1. Did this study report adverse events?

Yes (inclueds a explicite report of no adverse events)

Harm	Describe
Imaging delay	2.
Need for additional imaging	3.
Fluid overload	4.
Heart failure	5.
Anaphalaxis	6.
7. Other	8.

Cochrane Risk of Bias

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Rethnam U, Yesupalan RS, Sinha A.

Submit Form and go to or Skip to Next

Risk of Bias

1. Choose primary outcome (if study has more than 1 primary/main outcome, this form will need to be filled out multiple times).

Select an Answer

The full Cochrane Riskl of Bias tool can be accessed here: http://ohg.cochrane.org/sites/ohg.cochrane.org/files/uploads/Risk%20of%20bias%20assessment%20tool.pdf

Please refer to the link above while performing RoB assessments

Domain	Desription	Review Author's Judgement ...does the study:
Sequence Generation	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	2. Was the allocation sequence adequately generated? Select an Answer
Allocation Concealment	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during enrollment.	3. Was allocation adequately concealed? Select an Answer
Blinding of Participants, Personnel, ad Outcome Assessors *Assessments should be made for each main outcome or class of*	Describe all measures used, if any to blind study personnel and participants from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	4. Was knowledge of the allocated intervention adequately prevented during the srudy? Select an Answer

outcomes		
Incomplete Outcome Data *Assessments should be made for each main outcome or class of outcomes*	Describe the completeness of outcome data for each main outcome, including attrition and exclusion from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compare with total randomized participants), reason for attrition/exclusions where reported, and any re-inclusions in analyses performed by teh review authors.	5. Were incomplete oucome data adequately addressed? Select an Answer
Selective Outcome Reporting	State how the possibility of selective outcome reporting was examined by the review authors, and what was found	6. Are reports of the study free of suggestion of selective outcome reporting? Select an Answer
Other Sources of Bias	State any important concerns about bias not addresses in the other domains in the tool.	7. Was the study apparently free of other problems that could put it at a high risk of biase? Select an Answer

8. Comments

9. **R2 only: if you are reviewing R1 data entry, enter your initials when you have completed the audit**

Submit Form and go to or Skip to Next

Appendix D: List of Excluded Studies

Exclusion: Abstract Only.

M. R. Gandhi, P. Brown, C. A. Romanowski, S. K. Morcos, S. Campbell, A. M. el Nahas and T. A. Gray. The use of theophylline, an adenosine antagonist in the prevention of contrast media induced nephrotoxicity. Br J Radiol. 1992. 65:838

M. S. Davenport, S. Khalatbari, N. R. Dunnick, J. R. Dillman and J. H. Ellis. Contrast-induced nephrotoxicity: Risk of intravenous low osmolality iodinated contrast material stratified by estimated glomerular filtration rate. Abdominal Imaging. 2013. 38:628

J. Sugioka, M. Inagaki, S. Fukuzawa, A. Ikeda, S. Okino, J. Maekawa, S. Maekawa, S. Ichikawa, N. Kuroiwa and S. Okamoto. Risk prediction of contrast-induced nephropathy in diabetic patients undergoing primary percutaneous coronary intervention for acute myocardial infarction. Cardiology (Switzerland). 2013. 125:164

M. Fujimoto, K. Waseda, H. Takashima, K. Maeda, K. Asai, Y. Kuroda, T. Kosaka, A. Kurita, Y. Kuhara, H. Ando, S. Sakurai, D. Kato, A. Suzuki, Y. Nakano, T. Niwa, K. Mukai, S. Sato, T. Mizuno and T. Amano. Effect of oral hydration on renal function after coronary catheterization. American Journal of Cardiology. 2013. 111:89B

M. Habib, A. Hillis and A. Hamad. The role of ascorbic acid or n-acetylcysteine or combination in prevention of contrast-induced nephropathy in high-risk patients with ischemic heart disease. International Journal of Cardiology. 2013. 163:S64

M. Habib, A. Hillis and A. Hamad. Low dose of N-acetylcysteine plus ascorbic acid versus hydration with (saline 0.9%) for prevention of contrast-induced nephropathy in patients undergoing coronary angiography. International Journal of Cardiology. 2013. 163:S81

S. Hamdi, W. Selmi, A. Hraiech, W. Jomaa, K. B. Hamda and F. Maatouk. Prevention of contrast induced nephropathy in patients undergoing coronarography with ascorbic acid. JACC: Cardiovascular Interventions. 2013. 6:S22

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Appendix E. Evidence Tables for Main Comparisons

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN.

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
ACT, 2011[1]	General	Total		2308	30 Days	NR	NR	NR	NR	NR
		1	Placebo	1136		447(39.3)	68.1	NR	NR	NR
		2	Acetylcysteine	1172		445(38)	68	NR	NR	NR
Alioglu, 2013[2]	General	Total		113	NR	NR	NR	NR	NR	NR
		1	Control	49		(34.4)	60.84	NR	NR	NR
		2	NAC	64		(32.7)	62.73	NR	NR	NR
Allaqaband, 2002[3]	General	Total		123	48 hrs	52(42)	71	NR	NR	NR
		1	0.45% Saline	40		16(67)	71	NR	NR	NR
		2	0.45% Saline + NAC	45		17(38)	70	NR	NR	NR
		3	0.45% Saline + Fenoldopam	38		19(50)	71	NR	NR	NR
Amini, 2009[4]	Chronic kidney disease, defined as SrCr concentration ≥ 1.5 mg/dL for men and ≥ 1.4 mg/dL for women	Total		90	48 hrs	NR	NR	NR	NR	NR
		1	Placebo	45		11(24)	65.09	NR	NR	NR
		2	N-Acetylcysteine	45		25(56)	63.25	NR	NR	NR
Aslanger, 2012[5]	STEMI, ST-segment elevation myocardial infarction,	Total		312	72 hrs	NR	NR	NR	NR	NR
		1	Placebo	99		23(26)	57.2	NR	NR	NR
		2	IV NAC	108		22(20)	56.1	NR	NR	NR
		3	Intra-renal NAC	105		23(22)	55.9	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Awal, 2011[6]	SrCr ≥ 1.2mg/dl	Total		100	24 hrs	NR	NR	NR	NR	NR
		1	IVF Normal saline	50		10(20)	52;Range: 32-80	NR	NR	NR
		2	IVF Normal saline+N acetylcysteine	50		8(16)	58;Range: 38-76	NR	NR	NR
Azmus, 2005[7]	General	Total		397	48 hrs	NR	NR	NR	NR	NR
		1	Placebo	201		84(41.8)	67	NR	NR	NR
		2	NAC	196		79(40.3)	66	NR	NR	NR
Baker, 2003[8]	General	Total		80	Mean 96 hrs	10	NR	NR	NR	NR
		1	Saline only	39		6	67.4	NR	NR	NR
		2	IV saline + NAC	41		4	67.4	NR		NR
Baskurt, 2009[9]	Moderate degree chronic kidney disease with eGFR between 30 and 60 mL min1.73 m2	Total		217	12 Months	87	67.4	NR	NR	NR
		1	Hydration	72		31	67.1	NR	NR	NR
		2	Hydration + N-acetylcysteine	73		27	67.9	NR	NR	NR
		3	Hydration + N-acetylcysteine + theophylline	72		29	67.1	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Bilasy, 2012[10]	Moderate risk for CIN, moderate risk for CIN as defined by Mehran risk score	Total		60	72 hrs	NR	NR	NR	NR	NR
		1	IVF NaCl	30		15(50)	57.23	NR	NR	NR
		2	Theophylline	30		9(30)	56.8	NR	NR	NR
Boccalandro, 2003[11]	General	Total		179	48 hrs	NR	NR	NR	NR	NR
		1	No acetylcysteine + hydratrion	106		47	66	NR	NR	NR
		2	Acetylcysteine + hydration	73		24	66	NR	NR	NR
Boucek, 2013[12]	Presence of diabetes upon enrollment, SrCr > 100 umol/L (>1.136 mg/dl)	Total		120	2 Days	NR	NR	NR	NR	NR
		1	NaCl	59		15(34.1)	67	NR	NR	NR
		2	NaHCO3	61		15(32.6)	63	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Brar, 2008[13]	Stable renal disease(not defined)	Total		323	6 Months	NR	NR	NR	NR	NR
		1	NaCl	165		62 (35.2)number and % females applies to total randomized population before exclusions due to loss to f/u and protocol violations	Median, 71 ; Range, 65-76	NR	NR	NR
		2	NaHCO3	158		66 (37.7)	Median, 71 ; Range, 65-75	NR	NR	NR
Briguori, 2002[14]	Cr >1.2mg/dl, creatinine clearance <70ml/min	Total		183	5 Days	NR	NR	NR	NR	NR
		1	Control	91		10(11)	64+/-9	NR	NR	NR
		2	NAC	92		15(16)	64+/-9	NR	NR	NR
Brueck, 2013[15]	General	Total		499	72 hrs	NR	NR	NR	NR	NR
		1	Placebo	198		75(37.9)	74; Range: 69-77	NR	NR	NR
		2	N-Acetylcysteine	199		69(34.7)	75; Range: 70-79	NR	NR	NR
		3	Ascorbic Acid	102		37(36.3)	75; Range: 69-79	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Burns, 2010[16]	General	Total		42	5 Days	NR	NR	NR	NR	NR
		1	Placebo	21		NR	NR	NR	NR	NR
		2	NAC	21		NR	NR	NR	NR	NR
Carbonell, 2007[17]	General	Total		216	48 Hours	NR	NR	NR	NR	NR
		1	Placebo	109		30(27.5)	63.1+/-13.7	NR	NR	NR
		2	NAC	107		21(18.6)	63.1+/-13.7	NR	NR	NR
Carbonell, 2010[18]	SrCr >1.4	Total		0	2 Days		NR	NR	NR	NR
		1	Placebo	42		8(19)	NR	NR	NR	Current: 19(43)
		2	NAC	39		8(20)	NR	NR	NR	Current: 24(61)
Castini, 2010[19]	General	Total		156	5 Days	NR	NR	NR	NR	NR
		1	IV saline	51		8 (16)	72.7+/-8.2	NR	NR	NR
		2	IV saline + NAC	53		3 (6)	70.5+/-7.2	NR	NR	NR
		3	IV sodium bicarb	52		8 (15)	70.0+/-83.	NR	NR	NR
Chousterman, 2011[20]	General	Total		116	72 hrs	NR	NR	NR	NR	NR
		1	Usual care, No NAC	54		NR	65 (50-72)	NR	NR	NR
		2	NAC	62		NR	63 (47-73)	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Chousterman, 2013[21]	ICU patients	Total		140	72 hrs	NR	NR	NR	NR	NR
		1	Saline	70 54 patients but 70 radiological examinations		NR	Median: 63; Range: 47-73	NR	NR	NR
		2	NAC	70 while Arm 2 had 62 patients with 70 radiological examinations		NR	Median: 65;Range: 50-72	NR	NR	NR
Demir, 2008[22]	General	Total		97	3 Days	43(44)	NR	NR	NR	NR
		1	Saline	20		5(25)	58+/-11.3	NR	NR	NR
		2	Saline + NAC (NAC)	20		9(45)	62.0+/-15.8	NR	NR	NR
		3	Saline + Misopriatol (M)	20		11(55)	56.5+/-13.0	NR	NR	NR
		4	Saline + Theophylline (T)	20		9(45)	56.3+/-13.0	NR	NR	NR
		5	Saline + Nifedipine(N)	17		9(53)	60.1+/-10.7	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Durham, 2002[23]	Baseline SrCr >1.7 mg/dL.	Total		79	144 hrs	NR	NR	Reported	NR	NR
		1	IV hydration plus placebo	41		13	69.8	White: 36 Black: 2 Latino: 3 Other: 0	NR	NR
		2	IV hydration plus NAC	38		14	71.4	White: 32 Black: 4 Latino: 1 Other: 1	NR	NR
Ferrario, 2009[24]	Moderate to severe chronic renal failure: <55ml/min creatinine clearance	Total		200	3 Days	NR	NR	NR	NR	NR
		1	Placebo	101		38(38)	75	NR	NR	NR
		2	NAC	99		32(32)	75	NR	NR	NR
Frank, 2003[25]	Patients with chronic renal insufficiency, not yet dialysis dependent	Total		17	8 weeks	NR	NR	NR	NR	NR
		1	0.9% saline volume expansion	10		1	57.6+/-12.4	NR	NR	NR
		2	0.9% saline volume expansion + high-flux HD	7		2	66.8+/-9.2	NR	NR	NR
Fung, 2004[26]	Moderate to severe renal impairment: SrCr 1.69 -4.52mg/dl (149-400umol/L)	Total		91	NR		NR	NR	NR	NR
		1	IV hydration+ No drug	45		15(33)	68.0	NR	NR	NR
		2	IV hydration +NAC	46		12(26)	68.2	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Goldenberg, 2004[27]	Chronic renal insufficiency (mean [±SD] serum creatinine concentration 2.0±0.39 mg/dl)	Total		80	7 Days	NR	NR	NR	NR	NR
		1	Placebo plus IV saline 0.45%	39		8	69	NR	NR	NR
		2	Acetylcysteine plus IV saline 0.45%	41		6	71	NR	NR	NR
Gomes, 2005[28]	At risk for developing CIN, considered to be at risk for developing CIN if they had one of the following criteria: serum creatinine > 106.08 mmol/l, creatinine clearance (CrCl) , 50 ml/min, or drug treated diabetes mellitus	Total		156	48 Hours	NR	NR	NR	NR	NR
		1	Placebo	79		(43)	66.5	NR	NR	NR
		2	N-Acetylcysteine	77		(39)	63.8	NR	NR	NR
Gomes, 2012[29]	SrCr, >1.2mg/dl, GFR, <50ml/min	Total		301	48 hrs	NR	NR	NR	NR	NR
		1	Saline solution	151		(25.2)	64.5	Black: (16)	NR	NR
		2	NaHCO3	150		(30.7)	64.1	Black: (14.9)	NR	NR
Gulel, 2005[30]	Cr>1.3	Total		50	48 hrs	NR	NR	NR	NR	NR
		1	Control	25		(28)	61.5+/-11.6	NR	NR	Current: (42)
		2	NAC	25		(20)	61.4+/-12.3	NR	NR	Current: (38)

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Gunebakmaz, 2012[31]	General	Total		120	5 Days	NR	NR	NR	NR	NR
		1	Saline	40		15	66.4 +/- 10.7	NR	NR	NR
		2	Saline + Nebivolol	40		11	64.1+/- 9	NR	NR	NR
		3	Saline + NAC	40		11	64.7 +/- 11.9	NR	NR	NR
Han, 2013[32]	CKD, undefined	Total		2998	72 hrs	NR	NR	NR	NR	NR
		1	Usual care	1500		509 (43.9)	61.44	NR	NR	Current: 491 (32.7)
		2	Rosuvastatin	1498		535 (65.7)	61.45	NR	NR	Current: 463 (30.9)
Heguilen, 2013[33]	General	Total		0	3 Days	NR	NR	NR	NR	NR
		2	NaHCO3	47		15	67.7	NR	NR	NR
		3	NAC	44		11	64.8	NR	NR	NR
		4	NAC + saline	42		8	69.3	NR	NR	NR
Holscher, 2008[34]	General	Total		412	30 Days	NR	NR	NR	NR	NR
		1	hydration only	139		68(16.5)	67.1	NR	NR	NR
		2	hydration plus dialysis	134		58(15.5)	66.8	NR	NR	NR
		3	hydration plus NAC	139		10(26.3)	70.5	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Hsu, 2007[35]	SrCr >=1.6mg/dl or eGFR< 40ml/mi, Diabetic patients	Total		20	5 Days	NR	NR	NR	NR	NR
Hsu, 2007		1	IV Hydration + Placebo	9		6(66.6)	48-78	NR	NR	NR
		2	IV hydration + N-acetylcysteine	11		4(36.4)	44-84	NR	NR	NR
Hsu, 2012[36]	General	Total		240	NR	NR	NR	NR	NR	NR
		1	control	103		25(24.3)	79.7	NR	NR	NR
		2	NAC	106		28(26.4)	79.7	NR		NR
Izani Wan Mohamed, 2008[37]	Renal impairment-mean SrCr 124.1+/-19.68umol/l	Total		100	48 hrs	NR	NR	NR	NR	NR
		1	IV hydration	51		9(17.6)	56.4	NR	NR	NR
		2	IV hydration + oral NAC	49		7(14.3)	57.64	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Jaffery, 2012[38]	Myocardial infarction (MI):(1) typical rise and fall of biochemical markers of myocardial necrosis (troponin-I >0.026 IU or CK-MB 4% of total CPK) with at least one of the following: (a) symptoms of coronary ischemia; (b) development of pathologic Q-waves on the electrocardiogram; or (c) electrocardiographic changes indicative of myocardial ischemia (ST segment elevation or depression), Unstable angina (UA), UA was defined by at least one of the following: (1) angina that occurs at rest and is prolonged >20 minutes; (2) new-onset angina of at least Canadian Cardiovascular Society (CCS) Class III severity; (3) previously diagnosed angina that has become distinctly more frequent, longer in duration, or lower in threshold (increased by 1 CCS class to at least CCS Class III severity)., ACS, MI and UA	Total		398	NR	146(36.7)	65.4	White: 269(67.6) Black: 108(27.1) Other: 17(4.3)	NR	Current: 84(21.1)
		1	Hydration	192		78(40.6)	65.6	White: 129(68.6) Black: 52(27.7) Other: 7(3.7)	NR	Current: 44(22.9)
		2	NAC	206		68(33)	65.6	White: 140(68) Black: 56(27.2) Other: 10(4.9)	NR	Current: 40(19.4)

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Jo, 2008[39]	High risk population of patients with renal insufficiency undergoing coronary angiography. Creatinine clearance < 60ml/min	Total		247	6 Months	NR	NR	NR	NR	NR
		1	Placebo	123		NR	66.1	NR	NR	NR
		2	Simvastatin	124		NR	65.0	NR	NR	NR
Kay, 2003[40]	Cr >1.2mg/dl- CrCl<60ml/min	Total		200	7 Days	NR	NR	NR	NR	NR
		1	Placebo	98		36(37)	Median: 69;Range: 48-82	NR	NR	NR
		2	NAC	102		41(40)	Median: 69;Range: 50-81	NR	NR	NR
Kefer, 2003[41]	General	Total		104	24 hrs	NR	NR	NR	NR	NR
		1	pPlacebo	51		12	61	NR	NR	NR
		2	NAC	53		12	61	NR	NR	NR
Khalili, 2006[42]	SrCr concentration above 1.2mg/dl or creatinine clearance of less than 60 ml/min	Total		70	72 hrs	NR	NR	NR	NR	NR
		1	Saline	35		13	74	NR	NR	NR
		2	NAC + saline	35		15	74	NR	NR	NR
		3	0	0		NR	NR	NR	NR	NR
		4	0	0		NR	NR	NR	NR	NR
Kim, 2010[43]	General	Total		166	48 hrs	NR	NR	NR	NR	All: (37)
		1	Control	86		(42)	62	NR	NR	NR
		2	NAC	80		(37)	62	NR	NR	NR
Kimmel, 2008[44]	Mild to moderately impaired kidney function: SrCr ≥ 1.2 mg/dl or a creatinine clearance < 50 ml/min	Total		54	2 Days	NR	NR	NR	NR	NR
		1	Placebo	17		(30)	66.8	NR	NR	NR
		2	NAC	19		(21)	71.5	NR	NR	NR
		3	Zinc	18		(28)	67.2	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Kinbara, 2010[45]	Stable coronary artery disease	Total		45	48 hrs	NR	NR	NR	NR	NR
		1	Hydration	15		6 (40)	70	NR	NR	NR
		2	Hydration and aminophylline	15		5 (33)	71	NR	NR	NR
		3	Hydration and N-acetylcysteine	15		6 (40)	70	NR	NR	NR
Koc, 2013[46]	Use of oral hypoglycemic agents or insulin, fasting plasma glucose levels greater than 126 mg/dL, or a random plasma glucose level of 200 mg/dL or greater.	Total		195	48 hrs	NR	NR	NR	NR	NR
		1	Normal saline	101		53(52)	62	NR	NR	Current: 26(26)
		2	NaHCO3	94		40(42)	62	NR	NR	Current: 31(33)
Kotlyar, 2005[47]	SrCr concentrations ≥0.13 mmol/l	Total		60	30 Days	NR	NR	NR	NR	NR
		1	IV hydration	19		2(10)	69	NR	NR	NR
		2	NAC 300mg	20		5(25)	66	NR	NR	NR
		3	NAC 600mg	21		3(14)	67	NR	NR	NR
Lee, 2011[48]	General	Total		382	6 Months	NR	NR	NR	NR	NR
		1	Saline	189		54(28.6)	Median: 68.5;Range : 62-72	NR	NR	NR
		2	NaHCO3	193		57(29.5)	Median: 68.5; Range: 63-73	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Lehnert, 1998[49]	Stable SrCr of at least 1.4 mg/dl	Total		30 34 patients randomized, 4 dropped out within the first 24 hrs.	14 days	NR	NR	NR	NR	NR
		1	Saline	15		2	63.3	NR	NR	NR
		2	Hemodialysis	15		3	60.1	NR	NR	NR
Li, 2012[50]	Acute STEMI, symptoms of ischemic chest pain lasting for at least 20 min, which could not be relieved by oral nitrates, with new ST- segment elevation with the cut-off points >= 1 mm in >= 2-standard leads or >= 2 mm in >= 2-contiguous precordial leads on electrocardiogra m or left bundle branch block , with or without the elevation of cardiac enzymes.	Total		161	72 hrs	NR	NR	NR	NR	NR
		1	control	83		19(32.9)	66.3	NR	NR	Current: 50(60.2)
		2	atorvastatin	78		20(75.6)	66.3	NR	NR	Current: 47(60.3)
MacNeill, 2003[51]	SrCr greater than or equal to 1.5 mg/dl at morning of procedure	Total		43	NR	6	72.5 +/- 9.5	NR	NR	NR
		1	Placebo	22		1	72.9 +/- 10.3	NR	NR	NR
		2	NAC	21		5	72.1 +/- 8.8	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Marenzi, 2003[52]	Chronic renal failure, SrCr>2.0 mg/dl	Total		114	12 Months	NR	NR	NR	NR	NR
		1	Isotonic saline	56		13 (23)	69+/-11	NR	NR	NR
		2	Hemofiltration therapy	58		12 (21)	69+/-10	NR	NR	NR
Marenzi, 2006[53]	Acute MI, ST segment elevation acute MI	Total		354	NR	NR	NR	NR	NR	NR
		1	placebo	119		22(18)	62.5	NR	NR	Current: 60(50)
		2	Standard dose NAC	115		28(24)	62.5	NR	NR	Current: 57(50)
		3	High dose NAC	118		18(15)	62.2	NR	NR	Current: 77(65)
Marenzi, 2006[54]	Chronic kidney disease (creatinine clearance ≤30 mL/min)	Total		92	NR	NR	NR	NR	NR	NR
		1	isotonic saline	30		8 (27)	71	NR	NR	NR
		2	isotonic saline plus hemofiltration after contrast exposure	31		8 (26)	72	NR	NR	NR
		3	isotonic saline plus hemofiltration before and after contrast exposure	31		11 (35)	72	NR	NR	NR
Masuda, 2007[55]	SrCr concentration greater than 1.1mg/dl or estimated gfr less than 60ml/min	Total		59	2 Days	NR	NR	NR	NR	NR
		1	NaCl (control)	29		12 (41)	76	NR	NR	NR
		2	NaHCO3	30		11 (37)	75	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Matejka, 2010[56]	SrCr > 1.47mg/dL	Total		58	4 Days	NR	NR	NR	NR	NR
		1	Control	31		9(36)	Median: 75; Range: 71-77	NR	NR	NR
		2	Theophylline	27		13(42)	Median: 75;Range: 69-80	NR	NR	NR
Merten, 2004[57]	Stable renal insufficiency undergoing diagnostic or interventional procedures requiring radiographic contrast.	Total		119	2 Days	NR	NR	NR	NR	NR
		2	NaCl	60		16 (27)	66.7	NR	NR	NR
		3	NaHCO3	0		NR	NR	NR	NR	NR
Miner, 2004[58]	Moderate renal impairment	Total		180	at least 6 months post-procedure.	NR	NR	NR	NR	NR
		1	Placebo	85		(34)	69	NR	NR	Current: (10)
		2	NAC	95		(32)	71	NR	NR	Current: (7)
Motohiro, 2011[59]	GFR <60	Total		155	1 Months	NR	NR	NR	NR	NR
		1	Cl	77		28 (36)	74 +/- 7	NR	NR	Current: 37 (48)
		2	Bicarbonate	78		19 (24)	71 +/- 9	NR	NR	Current: 48 (61)
Ochoa, 2004[60]	Documented chronic renal insufficiency (SrCr >1.8 mg/dL (males), >1.6 mg/dL (females), or a calculated creatinine clearance <50 mL/min (Cockcroft-Gault formula)	Total		80	30 Days	NR	NR	NR	NR	NR
		1	Placebo	44		26(59)	70	NR	NR	NR
		2	NAC	36		20(56)	73	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Oldemeyer, 2003[61]	Creatinine clearance <50ml/min, or SrCr >1.2 mg/dl	Total		96	48 hrs	NR	NR	Reported	NR	NR
		1	Placebo	47		21	75+/-8	White: 45(96) Black: 2(4)	NR	NR
		2	NAC	49		22	77+/-9	White: 48(98) Black: 1(2)	NR	NR
Ozcan, 2007[62]	General	Total		264	2 Days	(25.4)	69;Range: 40-87	NR	NR	NR
		1	Saline	88		(25)	70;Range: 40-84	NR	NR	NR
		2	Saline + NAC	88		(23.9)	67;Range: 48-87	NR	NR	NR
		3	Bicarbonate	88		(27.3)	68;Range: 43-86	NR	NR	NR
Ozhan, 2010[63]	General	Total		130	48 hrs	53	54 +/-10	NR	NR	NR
		2	NAC	70		30	55+/-8	NR	NR	NR
		3	NAC + Atorvastatin	60		23	54+/-10	NR	NR	NR
Patti, 2011[64]	Acute coronary syndromes, unstable angina or non-ST-segment elevation myocardial infarction	Total		241	48 hrs	NR	NR	NR	NR	NR
		1	Placebo	121		25(21)	65 +/- 10	NR	NR	Current: 29(24)
		2	Atorvastatin	120		29(24)	65 +/- 10	NR	NR	Current: 39(32)
Poletti, 2007[65]	SrCr concentration > 106 µmol/L (1.2 mg/dL)	Total		100	4 Days	NR	NR	NR	NR	NR
		1	Hydration plus placebo	50		14(33)	72.7	NR	NR	NR
		2	Hydration plus N-acetylcysteine	50		18(41)	69.5	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Quintavalle, 2012[66]	General	Total		410	7 Days	NR	NR	NR	NR	NR
		1	Control	208		88(42)	70; Range: 8	NR	NR	NR
		2	Atorvastatin	202		99(49)	70; Range: 6	NR	NR	NR
Ratcliffe, 2009[67]	General	Total		78	7 Days	NR	NR	NR	NR	NR
		1	NaCl alone	15		6(40)	64	White: (20) Black: (27) Latino: (33) Asian/Pac: (20)	NR	NR
		2	NaCl plus NAC	21		10(48)	65	White: (10) Black: (33) Latino: (33) Asian/Pac: (20)	NR	NR
		3	NaHCO3 alone	19		8(42)	67	White: (6) Black: (44) Latino: (33) Asian/Pac: (24)	NR	NR
		4	NaHCO3 plus NAC	23		7(30)	65	White: (14) Black: (29) Latino: (43) Asian/Pac: (17)	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Reinecke, 2007[68]	General	Total		424	Median 553 Days Range 63-1316 days	NR	NR	NR	NR	NR
		1	Hydration only	140		24(17.1)	67.9	NR	NR	Ever: 80(57.1)
		2	Hydration + Dialysis	138		24(17.4)	67.9	NR	NR	Ever: 74(53.6)
		3	Hydration + NAC	146		25(17.1)	66.7	NR	NR	Ever: 75(51.4)
Sadat, 2011[69]	General	Total		40	7 Days	NR	75	NR	NR	NR
		1	IV Hydration only	19		NR	NR	NR	NR	NR
		2	Hydration+NAC	21		NR	NR	NR	NR	NR
Sandhu, 2006[70]	General	Total		106	48 hrs		NR	NR	NR	NR
		1	Control	53		22	66+/-13.9	NR	NR	NR
		2	NAC	53		18	69.3+/-14.2	NR	NR	NR
Seyon, 2007[71]	Renal dysfunction with baseline creatinine equal to or greater than 125 mol/L (1.4 mg/dL) for males or equal to or greater than 115 mol/L (1.3 mg/dL) for females	Total		40	NR	NR	NR	NR	NR	NR
		1	Placebo+hydration	20		6 (30)	74.7+/-9.7	NR	NR	NR
		2	N-Acetylcysteine+hydration	20		8 (40)	76.4+/-5.9	NR	NR	NR
Shavit, 2009[72]	Patients with CKD stage III–IV (eGFR 15–60mL/min	Total		93	48 hrs	NR	NR	NR	NR	NR
		1	NaHCO3	51		8(16)	71	NR	NR	Current: 11(22)
		2	NaCl + NAC	42		11(30)	71	NR	NR	Current: 9(25)

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Shyu, 2002[73]	SrCr concentrations 2.0 mg/dl and 6.0 mg/dl or rates of creatinine clearance (CrCl) 40 ml/min and 8 ml/min	Total		120	7 Days	NR	NR	NR	NR	NR
		1	Placebo + 0.45% saline	60		21(52.5)	70; Range: 63-77	NR	NR	NR
		2	NAC + 0.45% saline	60		18(42.8)	70; Range: 63-77	NR	NR	NR
Tanaka, 2011[74]	STEMI with PCI	Total		82	72 hrs	NR	NR	NR	NR	NR
		1	Placebo	38		7 (18)	60.5 +/- 14	NR	NR	Current: 9 (24)
		2	NAC	38		7 (18)	62.8 +/- 13	NR	NR	Current: 14 (42)
Tepel, 2000[75]	Known h/o CKD with stable creatinine defined as, SrCr concentration above 1.2 mg per deciliter (106 µmol per liter) or creatinine clearance of less than 50 ml per minute (0.8 ml per second)	Total	NR	83	6 days	36 (43)	NR	NR	NR	NR
		1	placebo and saline	42		19 (45)	65	NR	NR	NR
		2	Acetylcysteine (600 mg orally twice daily) and 0.45 percent saline intravenously	41		17 (41)	66	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Thiele, 2010[76]	Acute Myocardial Infarction, ST-segment elevation myocardial infarction patients	Total		251	one 6 months outpatient visit for all patients.	80(32)	NR	NR	NR	NR
		1	Placebo	125		43(34)	Median: 68;Range: 56-76	NR	NR	Current: 54(43)
		2	NAC	126		37(29)	Median: 68;Range: 57-75	NR	NR	Current: 40(32)
Toso, 2010[77]	General	Total		304	1 Month	NR	Median: 75	NR	NR	NR
		1	Placebo	152		60(40)	76 +/-7	NR	NR	NR
		2	Atorvastatin	152		48(32)	75+/-8	NR	NR	NR
Ueda, 2011[78]	Cr > 1.1 mg/dl - eGFR <60ml/min	Total		60	2 Days		75+/- 10	NR	NR	NR
		1	NaCl	30		7 (23)	77+/- 9	NR	NR	NR
		2	NaHCO3	30		NR	NR	NR	NR	NR
Vasheghani-Farahani, 2010[79]	CHF	Total		72	2 Days	NR	NR	NR	NR	NR
		1	Saline	36		7(19.4)	61.4	NR	NR	NR
		2	Bicarbonate	36		8(22.2)	61.4	NR	NR	NR
Vogt, 2001[80]	Chronic stable renal failure: >2.3 mg/dl SrCr	Total		113	NR	NR	NR	NR	NR	NR
		1	IV saline	58		23 (40)	69+/-10	NR	NR	NR
		2	IV saline/Hemodialysis	55		22 (40)	70+/-10	NR	NR	NR

Evidence Table 1. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status
Webb, 2004[81]	GFR < 50 ml/min	Total		487	Median: 3 Days	NR	NR	NR	NR	NR
		1	Placebo	245		(38.0)	70.0	NR	NR	Current: (9.4)
		2	NAC	242		(40.5)	70.8	NR	NR	Current: (11.3)
Xinwei, 2009[82]	Acute Coronary syndrome: ACS was defined as any one of the following: (1) unstable angina pectoris; (2) ST-segment elevation myocardial infarction; and (3) non–ST-segment elevation myocardial infarction	Total		228	48 hrs	NR	NR	NR	NR	NR
		2	Simvastatin 20	115		67 (58)	NR	NR	NR	NR
		3	Simvastatin 80	113		79 (70)	NR	NR	NR	NR

ACS=Acute Coronary Syndrome, AVH= amlodipine valsartan hydration group, CCS=Canadian Cardiovascular Society, CHF=Chronic Heart Failure, CIN=Contrast Induced Nephropathy, CKD=Chronic Kidney Disease, CK-MB=Creatine Kinase MB, CPK=Creatine Phosphokinase, Cr=Creatinine, CrCl=Creatinine Clearance, CRF=Chronic Renal Failure, eGFR=Estimated Glomerular Filtration Rate, GFR=Glomerular Filtration Rate, H=hydration group, HD=Hemodialysis, h/o=history of; hrs=hours; ICU=Intensive Care Unit, IU=International Units, IV=Intravenous, IVF=Intravenous Fluid, Mg/dl=milligram per deciliter, Mg/kg/hour=Milligram per kilogram per hour, Mg/kg=milligram per kilogram, MI=Myocardial Infarction, ml/min/1.73m^2=milliliter per minute per 1.73 meter squared, Ml/min=milliliter per minute, Mmol/l=millimole per liter, N=Sample Size, NAC=N-acetylcysteine, NR=Not Reported, NSTEMI=non-ST-segment elevation-mycordial infarction, OHT=Orthotopic Heart Transplantation, PCI=Percutaneous Coronary Intervention, SCr=SrCr, SD=Standard Deviation, SrCr=SrCr, STEMI= ST-segment elevation-mycordial infarction, UA=Unstalbe Angina, Ug/kg/min=microgram per kilogram per minute, Umol/l=micromole per liter
* if there is no “Arm 1” there is no control group.

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
ACT, 2011[1]	2	RCT/ Controlled	Yes	2008 to 2010	NR	Multi-center	PCI, mild-mod- Cr < 176 umol/L, Other Risk factors, GFR ≥60 to ≤89 and ≥30 to ≤59 No diagnostic coronary angiography due to either insignificant coronary lesions or bypass surgery. SrCr <176 µmol/L. No congestive heart failure (NYHA stage IV), or renal artery stenosis diagnosed with renal angiography incidentally during coronary angiography. No allergies to contrast agent or ACEI intolerance. No autoimmune disease, end-stage renal failure requiring dialysis, administration of contrast medium (CM) within the previous 6 days and within the following 2 days, or pregnancy.
Alioglu, 2013[2]	2	RCT/ Controlled	No	NR	NR	NR	>18 years, elective cardiovascular procedures; not on dialysis; NO patients with uncontrolled hypertension, SrCr levels of more than 7 mg/dL, severe valvular heart disease, autoimmune disease, chronic or acute infectious disease, emergency catheterization, recent exposure to radiographic contrast within 10 days, medication with NSAID or metformin up to 3 days before entering study, allergy to radiographic contrast or NAC
Allaqaband, 2002[3]	2	RCT/ Controlled	No	NR	Inpatient (including ICU)	NR	Scheduled to undergo cardiovascular intervention with radio contrast agent; baseline creatinine > 1.6 mg/dl or estimated CrCl 60 ml/min
Amini, 2009[4]	2	RCT/ Controlled trial	No	2006	Inpatient (including ICU)	Single-center	>18yrs; elective diagnostic coronary angiography; disease, defined as SrCr concentration ≥ 1.5 mg/dL for men and ≥ 1.4 mg/dL for women; Other Risk factors, history of diabetes mellitus for at least one year; no patients with acute coronary syndrome requiring primary or rescue coronary intervention within less than 12 h, no patients with cardiogenic shock, current peritoneal or hemodialysis, or a known allergy to NAC
Aslanger, 2012[5]	2	RCT/ Controlled	No	2007 to 2009	NR	Single-center	>30years, Primary angioplasty,; Other Risk factors, ST-segment elevation myocardial infarction, angioplasty within 12 hrs of symptoms No allergies to NAC Not on dialysis
Awal, 2011[6]	2	Non-RCT	No	2009 to 2010	Outpatient	Single-center	> 20 years Coronary angiography and intervention; SrCr <2 mg/dl. No acute myocardial infarction, unstable coronary syndrome, cardiogenic shock, history of end-stage renal failure or being on dialysis. No N-acetyl cysteine use and history of intravenous contrast media administration within the previous 10 days.
Azmus, 2005[7]	1,2	RCT/ Controlled	No	2001 to 2002	NR	NR	>70 years; Other Risk factors, Diabetic, SrCr levels >1.3 mg/dl. No dialyzed patients, no patients with acute renal failure
Baker, 2003[8]	2	RCT/ Controlled	Yes	NR	NR	Multi-center	Scheduled for coronary angiography; SrCr concentration >1.36 mg/dl or creatinine clearance <50 ml/min. No acute renal failure or end-stage renal failure on dialysis. Have not received a non-steroidal anti-inflammatory agent within 24 hrs of study. Those with blood pressure >90mm HG. No hemodynamically significant valvular heart disease. No signs of cardiac failure.

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Baskurt, 2009[9]	2	RCT/ Controlled	No	2008 to 2010	NR	Multi-center	>70year, coronary or peripheral arterial diagnostic intra- vascular angiography or percutaneous intervention chronic renal failure (stable SrCr concentrations >132.6 umol/L, at least 1 risk factor for contrast-induced acute kidney injury: age > 70 years, chronic renal failure (stable SrCr concentrations > 132.6 mol/L [1.5 mg/dL]), diabetes mellitus, clinical evidence of congestive heart failure, left ventricular ejection fraction < 0.45, or hypotension. no patient on dialysis and those with ST-segment elevation myocardial infarction undergoing primary angioplasty, no woman pregnant, breastfeeding, or aged 45years and not using contraceptive methods
Bilasy, 2012[10]	2	RCT/ Controlled	No	2009 to 2010	Inpatient (including ICU)	Single-center	Elective coronary angiography (CA) and/or angioplasty; moderate risk for CIN as defined by Mehran risk score, no subjects with unstable SrCr(defined as a difference of > 0.1 mg/dL between baseline "at admission" and preprocedural levels),no patients with recent intravascular administration of CM within 1 month, shock, end-stage renal disease on hemodialysis, and known hypersensitivity to NAC or theophylline, Serious cardiac arrhythmias, seizures, and acute renal failure
Boccalandro, 2003[11]	2	RCT/ Controlled	No	2000 to 2001	Inpatient (including ICU)	Single-center	Elective cardiac catheterization, SrCr 1.2 mg/dl or a creatinine clearance 50 ml who underwent elective cardiac catheterization and received 1 cc/kg of radiographic contrast, no acute renal failure or end-stage renal disease, not receiving oral theophylline, mannitol, furosemide, or dopamine, or undergoing renal angioplasty or renal angiogram
Boucek, 2013[12]	1,2	RCT/ Controlled	No	2008 to 2012	Inpatient (including ICU)	Single-center	Planned procedure using IV or IA contrast media; screening SrCr >100umol/L, Other Risk factors, Diabetic, Not on dialysis SrCr < 500umol/Lot an emergency procedure no acute kidney injury (> 50 umol/l) 24 hrs pre procedure no volume overload with left ventrictular failure systolic blood pressure < 180 mmHg hemodynamic stability with systolic blood pressure > or = to 90 mmHg and diastolic blood pressure > or = to 50 mmHg no contrast within 48 hrs of procedure not pregnant no other preventative CIN measures

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Brar, 2008[13]	2	RCT/ Controlled trial	No	2006 to 2007	Inpatient (including ICU)	Single-center	>18yrs; coronary angiography; Stable renal disease (not defined); other inclusion criteria were an estimated glomerular filtration rate (GFR) of 60 mL/min per 1.73 m 2 or less,and at least 1 of diabetes mellitus, history of congestive heart failure, hypertension (140/90 mm Hg or treatment with an antihypertensive medication), or age older than 75 years. Exclusion criteria included inability to obtain consent, receipt of a sodium bi- carbonate infusion prior to randomiza tion, emergency cardiac catheterization, intra-aortic balloon counter- pulsation, dialysis, exposure to radiographic contrast media within the preceding 2 days, allergy to radiographic contrast media, acutely decompensated congestive heart failure, severe valvular abnormality (eg, severe aortic stenosis or mitral regurgitation), single functioning kidney, history of kidney or heart transplantation, and change in estimated GFR of 7.5% or more per day or a cumulative change of 15% or more over the prior 2 or more days Patients were further stratified according to diabetes and N-acetylcysteine use
Briguori, 2002[14]	2	RCT/ Controlled	No	2006 to 2009	NR	Multi-center	>1<16 years,clinically indicated contrast-enhanced multi-detector computer tomography (MDCT), normal renal function (creatinine clearance >60 ml/min/1.73 m2, calculated by the Schwartz's formula),no case of pregnancy or known hypersensitivity to iodine-containing compounds, not received any iodinated contrast agent within 7 days before the administration of the investigational product, not scheduled to receive an iodinated contrast agent within 72 h after administration of the investigational product, not received any nephrotoxic medication (chemotherapeutic agents, diuretics or biguanide), no surgery planned within 72 h after the administration of the contrast agent.
Brueck, 2013[15]	2	RCT/ Controlled	No	2004 to 2008	Inpatient (including ICU)	Single-center	diagnostic or interventional cardiac catheterization, stable baseline SrCr concentration of ≥1.3 mg/dL, no SrCr measurements ≥0.3 mg/dL change in the 7 days prior to angiography, no exposure to contrast agents or nephrotoxic medication (ie, non-steroidal anti-inflammatory drugs, aminoglycoside, vancomycin) within the week prior to cardiac catheterization, no renal transplant recipients, plasmocytoma, oxalosis, nephrolithiasis, hyperthyroidism, unavailability of adequate time prior to angiography to perform the study procedures, no previously known insensitivity to N-acetylcysteine or ascorbic acid, no pregnant and breast feeding women, as well as those with child-bearing potential not using an approved method of contraception
Burns, 2010[16]	1	RCT/ Controlled	No	2002 to 2005	Inpatient (including ICU)	Multi-center	had a central venous access and a foley catheter, required a contrast-enhanced CT of any organ system; a SrCr of106 µmol/l and/or urea 6 mmol/l, urine output of < 0.5 cc/kg over 4 h or an increase in SrCr of 50 µmol/l in 24 h. Creatinine kinase <5000. No presence of myoglobunaria. No allergies to NAC or contrast. No serious illness with imminent threat of death. Not pregnant. No radiogenic shock. No nephritic, nephrotic or pulmonary-renal syndromes. No post-renal etiology of renal impairment. No previous renal transplant or solitary kidney. SrCr < 200 umol/l.

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Carbonell, 2007[17]	2	RCT/ Controlled	No	2002 to 2005	Inpatient (including ICU)	Single-center	Cardiac catheterization; Cr<1.4, no chronic renal failure, no acute renal dysfunction, no hemodynamic instability (systolic blood pressure <90 mm Hg), no known allergy to N - acetylcysteine or to contrast agents, no untreated gastrointestinal bleeding and/or previous treatment with theophylline, mannitol or nephrotoxic antibiotic
Carbonell, 2010[18]	2	RCT/ Controlled	No	2002 to 2006	Inpatient (including ICU)	Single-center	Coronary angiography; Cr >1.4, no hemodynamic instability (systolic blood pressure <90 mm Hg), no known NAC or contrast agent allergies, no untreated gastrointestinal bleeding, and/ or previous antibiotic treatment with theophylline, mannitol or nephrotoxic drugs
Castini, 2010[19]	2	RCT/ Controlled trial	No	NR	NR	NS	>18; cardiac aniogram; baseline creatinine level ≥1.2mg/dL; Stable SrCr: </= 4mg/dl; No history of dialysis; no multiple myeloma; no pulmonary edema; no cardiogenic shock; no acute MI; no emergency catheterization; no previous exposure to CM or NAC within 7 days; no previous enrollment in same or other protocols; not pregnant; no administration of theophylline, mannitol, dopamine, dobutamine, NSAIDS, or fenoldopam.
Chousterman, 2013[21]	1,2	Non-RCT	No	NR	Inpatient (including ICU)	Multi-center	All patients admitted into IOCU needing computed tomography or angiography; Patients free of dialysis. Available SrCr within 48 hrs before and 72 hrs after the radiological exam.
Chousterman, 2011[20]	1,2	RCT/ Controlled	No	NR	Inpatient (including ICU)	Multi-center	>18, needing computed tomography or angiography, No previous iodinated contrast within 3 days after index procedure.For NAC group, patient must have received at least one 600mg dose before examination.
Demir, 2008[22]	1	RCT/ Controlled	No	NR	Inpatient (including ICU)	Single-center	CT, No diabetes, no chronic renal failure, no uncontrolled hypertension or hypotension, no pregnancy, no ESRD, no renal transplantation, no dialysis history, no sensitivity to CM, no nephrotoxic drug use (NSAIDs, aminoglycoside, etc)
Durham, 2002[23]	2	RCT/ Controlled	No	NR	NR	Multi-center	>18years, coronary angiography and/or PCI, mild to moderate renal dysfunction with SrCr ≥ 1.1 mg/dL or creatinine clearance ≤ 60 mL/min, Does not have contrast-agent hypersensitivity, pregnancy-lactation, decompensated heart failure, pulmonary edema, emergency catheterization, acute renal failure or end-stage renal failure
Ferrario, 2009[24]	2	RCT/ Controlled	No	NR	NR	Single-center	>18 years, coronary or peripheral angiography/angioplasty, CVD; NYHA III-IV; creatinine clearance <55ml/min, No ongoing acute myocardial infarction or acute coronary syndrome. No need for theophylline, dopamine, fenoldopam, mannitol or nephrotoxic drugs within 1 week of procedure. No clinical signs of dehydration and systematic hypotension.
Frank, 2003[25]	2	RCT/ Controlled trial	No	2000 to 2001	Inpatient (including ICU)	Single-center	>18; coronary angiography; not requiring HD; Stable SrCr (> 3mg/dl); no allergy to contrast medium; not pregnant; no acute renal failure
Fung, 2004[26]	2	RCT/ Controlled	No	NR	NR	NR	elective coronary angiography or intervention; SrCr level of 1.69 to 4.52 mg/dL (149 to 400 umol /L), with at least 2 serum cr measurements within 1 month before coronary angiography, with fluctuation < 15% to confirm stable renal function before recruitment, No known allergy to NAC or contrast agents . Absence of cardiogenic shock, current dialysis therapy, and concomitant use of dopamine, theophylline, or mannitol.

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Goldenberg, 2004[27]	2	RCT/ Controlled	No	NR	NR	NR	Angiography Cr <1.5mg/dl and eGFR >70ml/min. No allergies to contrast media No renal insufficiency
Gomes, 2005[28]	2	RCT/ Controlled	No	2001 to 2003	Inpatient (including ICU)	Multi-center	Other Risk factors SrCr > 106.08 mmol/l, CrCl , 50 ml/min, or drug treated diabetes mellitus, no use of radiographic contrast media within 21 days of randomization, no current dialysis, no hemodynamic instability before the procedure (systolic blood pressure (90 mm Hg or diastolic blood pressure (60 mm Hg), and no history of sensitivity to N-acetylcysteine
Gomes, 2012[29]	2	RCT/ Controlled	No	NR	NR	Multi-center	Other Risk factors, SrCr >1.2mg/dl, or GFR <50 ml/min, No history of dialysis, no cardiac insufficiency class iii-iv, no emergency procedures, no use of contrast < 21 days ago.
Gulel, 2005[30]	2	RCT/ Controlled	No	NR	Inpatient (including ICU)	Single-center	Coronary angiography without intervention; Cr >1.3
Gunebakmaz, 2012[31]	2	RCT/ Controlled trial	No	2008 to 2009	NR	Single-center	coronary angiography or ventriculography; , excluded Baseline Creatinine > 1.2 mg/dl
Han, 2013[32]	2	RCT/ Controlled trial	No	2008 to 2011	NR	Multi-center	>18<75; undergoing coronary/peripheral artieral diagnostic angiography, left ventriculography or PCI; T2DM, defined by American Diabetes Association; CKD; did not receive statin treatment for at least 14 days prior to CM administration; no CM sensitivity; no T1DM; no ketoacidosis or lactoacidosis; CKD stage 2 or 3 only; no STEMI within 4 weeks of study; No class IV NYHA classification; hemodynamically stable; no CM 2 weeks prior to randomization; LDL >/= 1.82mmol.L; no hepatic dysfunction; no thyroid insufficiency; no renal artery stenosis
Heguilen, 2013[33]	1,2	RCT/ Controlled	No	NR	other	Single-center	> 18years, scheduled for cardiac catheterization or arteriographic procedure, Stable SrCr >1.25 mg/dL or Cockcroft-Gault-estimated creatinine clearance <45 ml/min non-emergency catheterization; without pulmonary edema; no preexisting dialysis; non recent exposure to CM; no history of multiple myeloma; controlled hypertensives; without hemodynamic instability; not being treated with the following medications: dopamine, mannitol, fenoldopam, aminophylline, theophylline, ascorbic acid or NAC; Non pregnant or childbearing women; or not hypersensitive to CM or NAC. The SCr shouldn't be [4.5 mg/dl ([364.5 lmol/l) or no change in SCr of at least 0.5 mg/dl (44.2 lmol/l) within the previous week.
Holscher, 2008[34]	2	RCT/ Controlled	No	NR	NR	Single-center	>14years and <79years, coronary angio-PCA- CT scan- IV pyelography; No acute renal failure, maintenance dialysis, history of acute myocardial infarction, left ventricular ejection fraction (EF) ≤ 25%, allergy to contrast media, pregnancy, contraindications for theophylline use such as untreated high-grade arrhythmia or history of seizure, or use of acetylcysteine.

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Hsu, 2007[35]	2	RCT/ Controlled	No	2003 to 2005	Outpatient	NR	Cardiac angiography; SrCr >1.6 mg/dL or eGFR <40ml/min, Other Risk factors, diabetes, left ventricular ejection fracture >40%, no acute coronary syndrome requiring immediate intervention, no end stage renal failure or unstable renal function, no shock, no unstable renal function, no active UTI, no acute renal failure or dialysis within last 30days, no heavy proteinuria (urinary protein >or = 300mg/dl) no gross hematuria, no active congestive heart failure, no exposure to contrast or other nephrotoxic agent in past 30days, no exposure to contrast media other than iohexol, no exposure to aminophylline, dopamine, or mannitol 1week before procedure, no SrCr measurement variation >15% 30days before procedure No HD and ARF
Hsu, 2012[36]	1	Non-RCT	No	2009 to 2010	Emergency department	Single-center	Abdominal or chest contrast-enhanced computed tomography, no long-term hemodialysis or peritoneal dialysis, Not received another dose of contrast medium within 72 hrs, no known allergy to N-acetyl- cysteine (NAC)
Huber, 2002[83]	1,2	RCT/ Controlled	No	NR	Referral from cardiology gastroenterology vascular surgery and urology services	Single-center	Stable serum cr of 1.3 mg/dL (114.3 umol /L) or higher, Non-pregnant women. No contraindication to theophylline such as untreated high-grade arrhythmia or history of seizure. Patients need to have a difference between measured baseline creatinine and creatinine obtained in the preceding 2 days of less than or equal to 0.3 mg/dl.
Izani Wan Mohamed, 2008[37]	2	RCT/ Controlled	No	2006 to 2007	Inpatient (including ICU)	Single-center	Coronary angiography; renal impairment-mean SrCr 124.1+/-19.68umol/l, calculated creatinine clearance between 40-90ml/min. No severe renal failure , No acute or reversible component of renal failure, no severe peptic ulcer disease, no history of allergy to N- acetyl cysteine No0 severe asthma, not pregnant or breast feeding.
Jaffery, 2012[38]	2	RCT/ Controlled	No	2007 to 2010	Inpatient (including ICU)	Single-center	>18 years, coronary angiography and/or percutaneous coronary intervention; NO end-stage renal disease (ESRD) requiring dialysis, NO known hypersensitivity to NAC, NO history of life threatening contrast reaction
Jo, 2008[39]	2	RCT/ Controlled trial	Yes	NR	NR	Multi-center	>19years; Coronary angiography; Creatinine clearance rates <60ml/min, Baseline SrCr >1.1mg/dl, no pregnancy, no lactation, no prior contrast media administration within 7 days of study entry, no emergent coronary angiography, no acute renal failure, no end-stage renal disease requiring dialysis, no history of hypersensitivity reaction to contrast media, no cardiogenic shock, no pulmonary edema, no multiple myeloma, no mechanical ventilation, no parenteral use of diuretics, no use of NAC or ascorbic acid, and use of metformin or nonsteroidal anti-inflammatory drugs within 48 hrs of the procedure no recent statin users (within 30 days before the procedure)

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Kay, 2003[40]	2	RCT/ Controlled	No	2006 to 2008	NR	Single-center	>21years estimated GFR between 30 and 60mlmin/1.73m^2 Patients with NO acute coronary syndrome, cardiogenic shock, chronic hemodialysis treatment, overt congestive heart failure, recent exposure to radio-contrast medium within preceding 14 days, emergent procedure. Patients NOT pregnant, patients with NO known allergy to NAC, theophylline or to contrast agents, contraindications to theophylline (history of seizures, arrhythmia resulting in haemodynamic instability and/or Lown classification (5A)or higher within 24 h before administration of contrast medium) and patients who were NOT taking any medication that has been shown exerting pharmacokinetic interaction with theophylline [cimetidine, isoproterenol (intravenous), salbutamol, terbutaline, corticosteroids, macrolide antibiotics, fluoroquinolones, rifampicin, isoniazid, phenytoin, carbamazepine, barbiturates, antacids (magnesium/aluminium hydroxide)]
Kefer, 2003[41]	2	RCT/ Controlled	No	NR	NR	NR	Undergoing coronary angiography or PCI; No renal dysfunction, Patients with SrCr concentration < 3mg/dl.
Khalili, 2006[42]	1,2	RCT/ Controlled	No	NR	NR	NR	SrCr concentration above 1.2 mg/dl or creatinine clearance of less than 60 ml/min, Stable SrCr, no acute renal failure, not treated with theophylline, calcium channel blockers, dopamine receptor agonists or diuretics.
Kim, 2010[43]	2	RCT/ Controlled	Yes	to	NR	Multi-center	>18years; coronary angiography; SrCr values: >1.5 mg/dl (132.6 umol/l) and =<3.0 mg/dl (265.2 umol/l),not pregnant, not lactating, left ventricular ejection fraction >20%, no hemodynamic instability, no acute MI, no planned staged interventional procedures, no participation in investigational drug study within 30 days, no severe liver disease, no allergy to iodinated CM, no jaundice or hematological disease, no scheduled renal angiography, no planned exposure to CM within 72 hrs, no intravascular admin of CM within previous 5 days, ability to return to lab at 48 and 72 hrs, no current intake of nephrotoxic drugs, no acute deterioration or fluctuation of renal function
Kimmel, 2008[44]	2	RCT/ Controlled	No	2005 to 2006	NR	Single-center	>18years, coronary angiography with or without PCI, not on dialysis; no acute renal failure or ESRD, no participation in an investigational drug or device trial within 30 days; not having received CM within 7 days of study entry; not scheduled major surgical intervention; no history of hypersensitivity reaction to iodinated CM; unstable hemodynamic conditions; use of N-acetylcysteine (NAC), metformin, or non-steroidal anti-inflammatory drugs within 48 hour to the procedure; intravenous use of diuretics or mannitol; and pregnancy or lactation. CrCl <60ml/min

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Kinbara, 2010[45]	2	RCT/ Controlled trial	No	2006 to 2007	Inpatient (including ICU)	Single-center	Coronary angiography; Other Risk factors, Stable coronary artery disease; Exclusion criteria of this study included acute myocardial infarction requiring primary or rescue PCI, use of vasopressors before PCI, cardiogenic shock, current peritoneal dialysis or hemodialysis, planned post-contrast dialysis, or allergies to the medications being studied
Koc, 2013[46]	2	RCT/ Controlled	No	2009 to 2010	NR	Multi-center	>18 years, undergoing coronary angiography or PCI; T2DM; use of oral hypoglycemic agents or insulin, fasting plasma glucose levels greater than 126 mg/dL, or a random plasma glucose level of 200 mg/dL or greater, No contrast-agent hypersensitivity, pregnancy lactation, decompensated heart failure, pulmonary edema or severe renal impairment (defined as SrCr [SCr] >3.0 mg/dL), emergency procedures. No previous contrast agent administration within 7 days of study enrollment.
Kotlyar, 2005[47]	2	RCT/ Controlled	No	NR	NR	Single-center	Elective coronary angiography and/or coronary intervention; no acute coronary syndrome requiring emergent coronary angiography or primary coronary intervention, no cardiogenic shock, no iodinated contrast media administration within a month or N -acetylcysteine within 48 h before the study entry, no current dialysis or a SrCr concentration N 1.4 mg/dL for men, or N 1.2 mg/ dL for women, no thyroid diseases, or no allergy to the study medication. Normal renal function (SrCr <1.4 mg/dl in men and <1.2 mg/dl in women)
Lee, 2011[48]	2	RCT/ Controlled	Yes	2008 to 2009	NR	Multi-center	>years 18years, coronary angiography; T2DM; Diagnosed with diabetes mellitus; SrCr >1.1 mg/dl but <9mg/dl. eGFR <60 ml/min/1.73m^2, but >15 ml/min/1.73m^2, Other Risk factors, No end stage renal disease on hemodialysis. No multiple myeloma, pulmonary edema or uncontrolled blood pressure. No acute ST-segment elevation myocardial infarction, emergency coronary angioplasty/angiography, contrast media within previous 2 days, pregnancy or allergies to contrast media/medications.
Lehnert, 1998[49]	1,2	RCT/ Controlled	No	NR	NR	Single-center	Angiography with at least 1.2 ml/kg/BW contrast medium dose (specific type of test was not listed as inclusion criterion); All patients with stable SrCr of at least 1.4mg/dl undergoing angiography with contrast medium dose of greater than or equal to 1.2ml/kg BW, non-pregnant women, no known allergy to contrast medium, no prior exposure to contrast medium in past 14 days before the start of the protocol, and no diagnosis of end-stage renal disease
Li, 2012[50]	2	RCT/ Controlled	No	2009 to 2011	Emergency department	Single-center	PCI; not on dialysis, ; Other Risk factors, acute STEMI, not on current or previous (<3 months) statin treatment, no history of renal and hepatic dysfunction, no prior fibrinolysis, unconsciousness at arrival, cardiogenic shock with intraaortic balloon pumping, uncontrolled hypertension (blood pressure >200/120 mm Hg) or stroke, a recent major operation (<3 months) or refusal to receive emergency PCI
MacNeill, 2003[51]	2	RCT/ Controlled	No	NR	NR	NR	Elective cardiac catheterization; SrCr greater or equal to 1.5 mg/dl on the morning of the planned procedure, Without Acute renal failure, without dialysis dependent chronic renal failure diagnosis, no exposure to contrast within the preceding 5 days, no pregnant women, no known sensitivity to NAC (no emergent procedures; the diagnostic test procedure is already labeled as "elective")

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Marenzi, 2006[53]	2	RCT/ Controlled	No	2003 to 2005	Inpatient (including ICU) other	Single-center	Primary angioplasty; Other Risk factors, AMI, Presented within 12 hrs (18hrs in cases of cardiogenic shock) after the onset of symptoms. Absence of long-term dialysis and known allergy to N-acetylcysteine.
Marenzi, 2003[52]	2	RCT/ Controlled trial	No	NR	Inpatient (including ICU)	Single-center	coronary angiography or elective percutaneous coronary intervention; chronic renal failure; SrCr > 2mg/dl and creatinine clearance < 50 mL/min; no acute coronary syndrome; no cardiogenic shock; no long-term peritoneal dialysis or HD treatment; no overt CHF; no recent major bleeds; no contraindications for anticoagulant therapy. enrolled patients with CRF who were scheduled for coronary angiography or an elective percutaneous coronary intervention at their institution.
Masuda, 2007[55]	2	RCT/ Controlled trial	No	2005 to 2006	Inpatient (including ICU)	Single-center	>20 years; Coronary angiography; SrCr greater than 1.1mg/dl or estimated glomerular filtration rate less than 60ml/min; no change in SrCr concentration of >/=0.5 mg/dl during the previous 24 hrs, no preexisting dialysis, no recent exposure to radiographic contrast media within 2 days of the study, no allergy to radiographic contrast media, no pregnancy, no previous or planned administration of mannitol, fenoldopam, N-acetylcysteine or nonstudy NaHCO3
Matejka, 2010[56]	2	RCT/ Controlled	No	2005 to 2008	Inpatient (including ICU) Outpatient	Single-center	>18years, coronary angiography or percutaneous coronary intervention,; Cr >/= 1.47mg/dl, Exclusion criteria were long-term dialysis, pregnancy, lactation, epilepsy, thyrotoxicosis, theophylline allergy, previous theophylline medication, arrhythmias with hemodynamic instability, severe liver dysfunction, clinical signs of dehydration and inability to take oral fluids. Use of angiotensin-converting enzyme inhibitors, non-steroidal anti-inflammatory drugs and other concomitant medications was left to the attending physician's discretion.
Miner, 2004[58]	2	RCT/ Controlled	No	NR	NR	Single-center	PCI or coronary angiography; Patients without diabetes with a calculated creatinine clearance (Cockcroft-Gault formula) <50 mL/min. Patients with diabetes were eligible if their calculated creatinine clearance was <100 mL/min. Any patient with an absolute SrCr >200 mol/L was eligible. Absence of renal replacement therapy (dialysis or transplantation, reactive airway disease requiring oral steroids, baseline systolic blood pressure <80 mm Hg. Absence of active congestive heart failure; No acute myocardial infarction (defined as ongoing chest pain with electrocardiographic changes); Not enrolled in another clinical trial; ability to provide informed consent; NO ongoing need for intravenous nitroglycerin; NO treatment with NAC within 72 hrs of planned PCI. Women not of childbearing age.
Motohiro, 2011[59]	2	RCT/ Controlled trial	No	2004 to 2007	Inpatient (including ICU)	Multi-center	>20years; coronary angiography; GFR <60 AND Cr < 4

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Ochoa, 2004[60]	2	RCT/ Controlled	No	NR	NR	Single-center	Elective or urgent coronary angiography and/or PCI; chronic renal insufficiency (SrCr >1.8 mg/dL (males), >1.6 mg/dL (females), or a calculated creatinine clearance <50 mL/min (Cockcroft-Gault formula, No recent (<6 weeks) elevation in SrCr >0.5 mg/dL, Not actively receiving any form of renal dialysis or dialysis planned post-angiography, No prior contrast media exposure within 48 hrs, No known allergy to N-acetylcysteine or history of anaphylaxis to intravenous contrast media, No recent decompensated congestive heart failure (<4 weeks), No cardiogenic shock or use of intravenous vasopressors within 1 week, No known or suspected severe aortic valve stenosis (area <1.0 m2, mean gradient >50 mmHg), and No recent (<4 weeks) initiation of diuretics or ACE inhibitors
Oldemeyer, 2003[61]	2	RCT/ Controlled	No	NR	NR	NR	>18 years and <80 years, Angiography history of chronic renal failure, stable SrCr concentrations >1.4 and <5.0mg/dl. No acute myocardial infarction, ARF, renovascular hypertension, prior vasopressor usage, cardiogenic shock and current peritoneal or hemodialysis.
Ozcan, 2007[62]	2	Dec_nRCT	No	NR	NR	NR	Coronary angiography and or percutaneous coronary intervention,; chronic renal insufficiency (mean [±SD] SrCr concentration 2.0±0.39 mg/dl), no patients with acute renal failure, acute myocardial infarction requiring primary or rescue coronary intervention within less than 12 h, cardiogenic shock, current peritoneal or hemodialysis, planned post-contrast dialysis, or a known allergy to acetylcysteine. SrCr >1.5 mg/dl or creatinine clearance of <50 ml/min.
Ozhan, 2010[63]	2	RCT/ Controlled	No	NR	NR	Single-center	Coronary or peripheral angiography and or PCI; CR > 1.5, creatinine clearance <60ml/min
Patti, 2011[64]	2	RCT/ Controlled	Yes	NR	NR	Multi-center	Undergoing PCI, CVD; unstable angina or non–ST-segment elevation myocardial infarction; Statin naive. No current or recent statin treatment (<3months). No non–ST-segment elevation ACS with high-risk features warranting emergency coronary angiography (<2 hrs), no any baseline increase in liver enzymes (aspartate aminotransferases/alanine aminotransferases), left ventricular ejection fraction >30%, renal failure with a creatinine level <3 mg/dl, and no history of liver or muscle disease.
Poletti, 2007[65]	1	RCT/ Controlled	No	NR	NR	NR	>19years, cath +/- PCI ; Cr >1.2 - CrCl<50ml/min, No acute kidney failure, were undergoing dialysis, or had unstable renal function as evidenced by a change in SrCr of 0.5 mg/dL or 25% in the prior 10 days. No known allergy to contrast or acetylcysteine, administration of mannitol, intravenous catecholamines, parenteral diuretics, theophylline, or a contrast agent within 7 days of study entry. No mechanical ventilation, cardiogenic shock, or emergent angiography.

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Quintavalle, 2012[66]	2	RCT/ Controlled	Yes	2005 to 2008	NR	NR	Undergoing coronary angiography, or PCI; eGFR < 60 ml/min/1.73m^2 enrolled in the Novel Approaches for Preventing or Limiting Events (NAPLES) II trial
Ratcliffe, 2009[67]	2	RCT/ Controlled	No	2007 to 2008	Inpatient (including ICU) Outpatient	Single-center	coronary angiography or coronary angioplasty; elevated SrCr (greater than 132.6 µmol/L in men, and greater than 114.9 µmol/L in women) or reduced calculated creatinine clearance (less than 1.002 mL/s) using the Cockcroft-Gault formula, Other Risk factors, DM on oral antiglycemic or insulin therapy, no acute MI, no Signs of heart failure or EF <35%, no cardiogenic shock, no hypertrophic or restriction cardiomyopathy, no contrast media exposure in last week, no previous reaction to contrast media, no renal transplantation, no dialysis, no severe comorbid illness, no use of dopamine, mannitol, or fenoldopam, no newly diagnosed uncontrolled DM, no inability to follow-up
Reinecke, 2007[68]	2	RCT/ Controlled	No	2001 to 2004	Inpatient (including ICU)	Single-center	Elective coronary angiography; SrCr concentrations ≥1.3 mg/dl and ≤3.5 mg/dl. Absence of acute or recent (within 30 days) myocardial infarction, congestive heart failure (New York Heart Association class IV), recipient of transplanted organs,monoclonal gammopathy, and/or previous contrast medium administration within 7 days
Sadat, 2011[69]	2	RCT/ Controlled	No	NR	NR	Single-center	Angiography +/- PCI,CVD; EF>35; ; Cr>1.2, creatinine clearance <60ml/min, No dialysis, acute renal failure, change in use of diuretic or antihypertensive agents or who had received contrast media within 30 days of entry. No congestive heart failure or severe valvular disease. No advanced left ventricular systolic dysfunction. Left ventricular ejection fraction >35%. No chronic lung disease or asthma exacerbation or allergy to acetylcysteine.
Sandhu, 2006[70]	2	RCT/ Controlled	No	2001 to 2002	Outpatient	NR	Renal-mesenteric or aortic angiography (noncoronary angiography);
Seyon, 2007[71]	2	RCT/ Controlled trial	No	NR	Inpatient (including ICU)	NS	>18yrs; coronary angiography; , baseline creatinine equal to or greater than 125 mol/L (1.4 mg/dL) for males or equal to or greater than 115 mol/L (1.3 mg/dL) for females; ACS, baseline SrCr 1.4 mg/dl (males) 1.3 mg/dl (females) or greater; no hemodynamic instability; not pregnant; no acute GI disorders; Killip class > III; NYHS < III; suitable to receive IV hydration; not sensitive to NAC; not receiving theophylline or manitol; not on dialysis; not in another study or using an experimental drug.
Shavit, 2009[72]	2	Non-RCT	No	2004 to 2007	NR	Single-center	>18 years; no preexisting dialysis, patients with CKD stage III–IV (eGFR 15–60mL/min), Patients with plasma creatinine levels more than 8 mg/dL or eGFR less than 15 mL/min, change in plasma creatinine levels of ≥0.5 mg/dL during the previous 24 hrs, multiple myeloma, pulmonary edema, uncontrolled hypertension (systolic>160 mmHg, diastolic >100 mmHg), recent exposure to radiographic contrast, or other nephrotoxic medications(within 2 days of the study), allergy to radio-contrast, or pregnancy were excluded.

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Shyu, 2002[73]	2	RCT/ Controlled	No	NR	NR	NR	Scheduled for cardiac angiography, serum creatinine concentrations 2.0 mg/dl and 6.0 mg/dl or rates of CrCl 40 ml/min and 8 ml/min, Other Risk factors, Stable creatinine levels: A difference of <0.1 mg/dl between baseline and follow-up at 2 weeks after procedure, Included if patient does not have acute myocardial infarction requiring primary or rescue coronary intervention, use of vasopressors before procedure, cardiogenic shock, current peritoneal dialysis or hemodialysis, planned post-contrast dialysis or allergies to the study medications.
Tanaka, 2011[74]	2	RCT/ Controlled trial	No	2007 to 2008	Inpatient (including ICU)	Single-center	Coronary angiogram
Tepel, 2000[75]	1	RCT/ Controlled	No	NR	NR	NR	history of chronic renal failure and with stable SrCr concentrations,No patient with acute renal failure was included
Thiele, 2010[76]	2	RCT/ Controlled	Yes	2000 to NR	NR	Single-center	coronary angiography +/- PCI; Cr >1.2 ,creatinine clearance <70ml.min
Toso, 2010[77]	2	RCT/ Controlled	No	to	Inpatient (including ICU)	Single-center	Computer tomography (CT) or digital subtraction- A total of 80 patients were enrolled. Forty patients tion angiography; creatinine >1.5mg/dl, supposed to receive at least 80 ml of a low-osmolality CM (iopromide) during procedure, no history of allergic reactions to CM or theophylline, no pregnancy, no uncontrolled arterial hypertension, no severe heart failure, no liver failure and no nephrotic syndrome
Ueda, 2011[78]	2	RCT/ Controlled trial	No	2008 to 2010	Emergency department	Single-center	>20years; coronary angiography or PCI; no SrCr change >/= 0.5 mg.dl within 24 hrs of procedure; no dialysis; no CM exposure 2 days prior to procedure; no CM allergy; not pregnant; no planned administration of mannitol, fenoldopam, NAC, theophylline, dopamine, or non-study sodium bicarb.
Vasheghani-Farahani, 2010[79]	2	RCT/ Controlled	No	2007 to 2008	Inpatient (including ICU)	Single-center	>18years coronary angiography,; SCr > 1.5, Uncontrolled hypertension CHF NYHA III-IV no unstable SrCr (change in creatinine concentration of at least 0.5 mg/dL or 25% from creatinine measured prior to the study to that of the day of angiography [baseline creatinine]); no previous history of dialysis; no eGFR <20 ml/min per 1.73 m 2 (calculated with the 4-variable Modification of Diet and Renal Disease Study equation) (15); no emergency catheterization; no recent exposure to radiographic contrast agents (within 2 days prior to the study); no allergy to contrast agent; no pregnancy; no administration of dopamine, mannitol, fenoldopam or N-acetylcysteine during the intended time of the study; no need for continuous hydration therapy (e.g., sepsis); and no multiple myeloma
Vogt, 2001[80]	1, 2	RCT/ Controlled trial	No	NR	Inpatient (including ICU)NR	Single-center	transluminal renal angioplasty, percutaneous transluminal angioplasty of the lower extremities, coronary angiography, CT, other radiographic investigation; chronic stable renal failure (SrCr > 2.3 mg/dL); Hardly any IC at all

Evidence Table 2. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria
Webb, 2004[81]	2	RCT/ Controlled	No	NR	NR	Multi-center	Undergoing diagnostic cardiac catheterization or percutaneous coronary intervention; GFR < 50 ml/min, GFR of <50ml/min, no suspected acute renal failure, Creatinine <400umol/l, not currently on dialysis, hemodynamic stability, No NAC administration within 48 hrs, and must be able to give informed consent and comply with follow-up.
Xinwei, 2009[82]	2	RCT/ Controlled trial	No	2007 to 2008	Inpatient (including ICU)	Single-center	Percutaneous Coronary Intervention; Other Risk factors, Acute Coronary Syndrome: ACS was defined as any one of the following: (1) unstable angina pectoris; (2) ST-segment elevation myocardial infarction; and (3) non–ST-segment elevation myocardial infarction; ; The following exclusion criteria were used: pregnancy, lactation, previous contrast media exposure within 7 days of study entry, acute renal failure, end-stage renal disease requiring dialysis, alanine transaminase elevation, history of hypersensitivity to contrast media, multiple myeloma, cardiogenic shock, and left ventricular ejection fraction 40%. Also, patients who had used statins within 30 days were excluded. Patients who had undergone primary PCI or had undergone PCI within 5 days after enrollment were excluded from the present study

ACE= Angiotensin Converting Enzyme, ACEI=Angiotensin Converting Enzyme Inhibitor, ACS=Acute Coronary Syndrome, AMI=Acute Myocardial Infarction, ARB=Angiotensin Receptor Blocker, ARF=Acute Renal Failure, AZ=Acetazolamide, BW=Body Weight, CABG=Coronary Artery Bypass Grafting, CAG= Coronary angiogram, Cc/kg=cubic centimeter per kilogram, CE-MDCT=Contrast Enhanced Multi-detector Computer Tomography, CHF=Chronic Heart Failure, CIN=Contrast Induced Nephropathy, CKD=Chronic Kidney Disease, CM=Contrast Media, Cr=Creatinine, CrCl=Creatinine Clearance, CRF=Chronic Renal Failure, CT=Computer Tomography, CVD=Cardiovascular Disease, EF=Ejection Fraction, eGFR=estimated Glomerular Filtration Rate, ESRD=Endstage Renal Disease, GFR=Glomerular Filtration Rate, GI=Gastrointestinal, H=hour, HD=Hemodialysis, IA=Intrarterial, ICU=Intensive Care Unit, IV=Intravenous, LDL=Low Density Lipoprotein, LVEF=Left Ventricular Ejection Fraction, MDCT=Multi-detector Computer Tomography, MDRD= Modification of Diet in Renal Diseases, mEq/l=milliequivalents per liter, Mg/dl=milligrams per deciliter, mg=milligram, MI=Myocardial Infarction, Ml/min/1.73m^2=milliter per minute per 1.73 meter squared, Ml/min=milliliter per minute, mmHG=millimeter of Mercury, Mol/l=mole per liter, NAC=N-acetylcysteine, NR=Not Reported, NSAID=Non-steroid Inflammatory Drug, NYHA=New York Heart Association, PCI=Percutaneous Coronary Intervention, PCr=Plasma Creatinine, RCT=Randomized Controlled Trial, SrCr=SrCr, STEMI= ST Elevation Myocardial Infarction, T2DM=Type 2 Diabetes Mellitus, Umol/l=micromole/liter, Yrs=years

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
ACT, 2011[1]	LOCM, IOCM, Other description, Also included high-osmolar contrast	IA	Not specified	1	Placebo	Oral	1200mg b.i.d, 4800mg total, 48 hrs, Prior to CM administration After CM administration	2 doses before and 2 doses after procedure Hydration with 0.9% saline, 1 ml/kg per hour, from 6 to 12 hrs before to 6 to 12 hrs after angiography, was strongly recommended
				2	Acetylcysteine	Oral	1200mg b.i.d, 4800mg total, 48 hrs, Prior to CM administration After CM administration	2 doses before and 2 doses after procedure
Alioglu, 2013 [2]	Iomeprol	IA	Not specified	1	Control	IV	IV infusion of 1 ml/kg/h with 0.45% saline for 24 h (12 h before and 12 h after exposure to contrast media, Prior to CM administration After CM administration	
				2	NAC	Oral, IV	Acetylcysteine 600 mg twice a day, on the day before and on the day of cardiovascular procedure, Prior to CM administration After CM administration	All patients received IV infusion of 1 ml/kg/h with 0.45% saline for 24 h (12 h before and 12 h after exposure to contrast media

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Allaqaband, 2002 [3]	LOCM	IA	Mean: Arm1 1.47 ml/kg (SD 0.90), Arm2 1.52ml./kg (SD 0.81), Arm3 1.63ml/kg (SD 0.67), Duration and volume not specified	1	0.45% saline	IV	0.45% Saline: 1 ml/kg/hr, 12 hour before procedure, during procedure, and 12 hrs after procedure, Prior , during CM, and after CM administration	
				2	0.45% saline + NAC	IV	Saline: 1 ml/kg/hr + NAC: 600mg 2x daily, Saline same as Arm 1, NAC: given 12 hrs before and 12 hrs after procedure, Prior to CM, during CM and after CM administration	
				3	0.45% saline + fenoldopam	IV	Saline: 1 ml/kg/hr + Fenoldopam: 0.1 microgram/kg/hr, Saline: same as Arm 1, Fenoldopam: starting 4 hrs before procedure and ending 4 hrs after, Prior to CM, during CM and after CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Amini, 2009[4]	Iodixanol, Iohexol	IA	Not specified	1	Placebo	Oral	NR, 24hrs before and 24hrs after, Prior and After CM administration	The patients were hydrated orally and intravenously. All the patients were encouraged to drink fluids like water and fruit juice for at least 8 glasses over 12 h before the procedure and memorize the number of glasses. The oral preprocedural hydration was estimated by multiplying the number of glasses drunk by 200 ml Patients were hydrated intravenously by 1 L of 0.9 normal saline, which was commenced in the catheterization laboratory
				2	N-acetylcysteine	Oral	600mg b.i.d, 24hrs before and 24hrs after, Prior and After CM administration	
Aslanger, 2012 [5]	Ioxaglate	IA	Not specified, Define, Mean: Arm1 - 204ml, Arm2 - 193ml, Arm3 - 205ml	1	Placebo	IV	12ml saline during procedure, placebo capsules presumably twice daily for 2 days, 48 hrs, During CM administration After CM administration	0.9% saline for 12 hrs at 1 ml/kg/hr
				2	IV NAC	IV	1200mg IV during procedure, 1200mg by mouth twice daily for 2 days, 48 hrs, During CM administration After CM administration	
				3	IA NAC	Other, IA	600mg IA before procedure, 1200mg by mouth twice daily for 2 days, 48 hrs, Prior to CM administration After CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Awal, 2011[6]	Not specified,	IA	Not specified	1	IVF Normal saline	IV	1ml/kg 12hrs before and 12hrs after procedure, 12hrs before and 12hrs after procedure, Prior to CM administration After CM administration	
				2	IVF Normal saline+ N acetylcysteine	Oral, IV	600mg NAC twice daily for 2 days plus control group treatment, Starting a day before procedure plus control group treatment, Prior to CM administration After CM administration	
Azmus, 2005 [7]	IA,	NR	Not specified	1	Placebo	Oral	600mg, 72 hrs, Prior to CM administration During CM administration After CM administration	2 doses prior to procedure, 2 doses day of procedure, 1 dose after procedure
				2	NAC	Oral	600mg, 72 hrs, Prior to CM administration During CM administration After CM administration	2 doses prior to procedure, 2 doses day of procedure, 1 dose after procedure
Baker, 2003 [8]	Iodixanol	IA	Not specified, Define, Mean: Arm1 222ml (SD 162), Arm2 238ml (SD 155)	1	Saline only	IV	Saline: 1ml/kg/h, 12 hrs pre-procedure and 12 hrs post-procedure, Prior to CM administration After CM administration	
				2	IV saline + NAC	IV	NAC: 150/mg/kg in 500ml saline, 4.5 hrs, Prior to CM administration After CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Baskurt, 2009[9]	LOCM, Ioversol	IA	Not specified	1	Hydration	IV	1 ml /kg/ h for 12 h before and after contrast exposure, 12 h before and after contrast exposure, Prior to CM administration After CM administration	
				2	Hydration + N-acetylcysteine	Oral, IV	1 ml /kg/ h of Isotonic Saline for 12 h before and after contrast exposure + NAC: 600 mg p.o. Twice daily the preceding day and the day of angiography, 12 h before and after contrast exposure, Prior to CM administration	
				3	Hydration + N-acetylcysteine + theophylline	Oral, IV	1 ml /kg/ h of isotonic saline for 12 h before and after contrast exposure.NAC + theophylline (600 mg NAC p.o. And 200 mg theophylline p.o. Twice daily for the preceding day and the day of angiography, 12 h before and after contrast exposure, Prior to CM administration	
Bilasy, 2012 [10]	Iopamidol, LOCM	IA	5 mL × body weight (kg)/SrCr level (mg/dL), Not specified	1	Placebo	IV	100 ml sodium chloride (0.9%) 30 minutes before the procedure, 30 minutes before the procedure, Prior to CM administration	All patients received 0.9% sodium chloride (1 mL/kg per hour) for 24 hours beginning 12 hours before the procedure. The only exception to this were patients with left ventricular ejection fraction (LVEF) <40% or in NYHA III–IV class (New York Heart Association functional class III–IV), where hydration rate was reduced to 0.5 mL/Kg per hour. All patients got NAC 600mg bd for the day before and day of the procedure There is no usual care arm. All patients also got NAC.

				2	Theophylline	IV	200 mg of theophylline in 100 ml NaCl (0.9%) intravenously 30 minutes before CM administration., 30 minutes before the procedure, Prior to CM administration	All patients got NAC 600mg bd for two days

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Boccalandro, 2003 [11]	Iodixanol	IA	2.3+/-1.5 mls/kg for control group and 2.3+/-1.7 for acetylcysteine group, Not specified, Define, 191+/-120 mls for control group and 192+/-142 for acetylcysteine group	1	No acetylcysteine+ hydratrion	IV Other, Did not receive acetylcysteine	.45% hallf normal saline 75cc/hr, 12 hrs before and after, Prior to CM administration During CM administration	Both groups had a standardized intravenous hydration regimen with half-normal saline (0.45%) at 75 cc/hr for 12 hr before and after the proce- dure.
				2	Acetylcysteine+ hydration	Oral, IV	600mg b.i.d acetylcysteine +.45% hallf normal saline 75cc/hr, day before and the day of the catheterization, Prior to CM administration During CM administration	.45% hallf normal saline 75cc/hr
Boucek, 2013 [12]	LOCM	IA or IV	Not specified, Define, Mean: 104ml for NaCl gorup, 115ml for NaHCO3	1	Sodium chloride	IV	154 ml of 8.4% NaHCO3 to 846 mls 5% glucose- 3 ml/kg x 1 hour, then 1 ml/kg/hr, 7 hrs, Prior to CM administration After CM administration	
				2	NaHCO3	IV	154 ml of 5.85% NaCl to 846 ml of 5% glucose-3 ml/kg x 1 hour, then 1 ml/kg/hr, 7 hrs, Prior to CM administration After CM administration	
Brar, 2008[13]	Ioxilan	IA	Not specified	1	NaCl	IV	3ml/kg before and 1.5ml/kg/hr during and after, 1hr before, during and 4hrs after procedure. Prior, during and after cm administration	
				2	NaHCO3	IV	3ml/kg before and 1.5ml/kg/hr during and after, 1hr before, during and 4hrs after procedure. Prior, during and after cm administration	
Briguori, 2002[14]	Iopromide	IA	Not specified	1	Control	NR	Normal saline, NR, Prior to CM administration After CM administration	All patients received saline 0.45% 1ml/kg/h infusion 12 h before-12h after CM
				2	Nac	Oral	NAC 600mg bid 2 days, 2 days, Prior to CM administration After CM administration	The day before and the day of the procedure

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Brueck, 2013 [15]	LOCM	IA	Not specified, Define, Median contrast volume was 110 mL (IQR, 80-160 mL) in the N-acetylcysteine group, 115 mL (IQR, 90-150 mL) in the ascorbic acid group, and 110 mL (IQR, 80-150 mL) in the placebo group	1	Placebo	IV	Placebo, over the course of 30 minutes, at 24 hrs and 1 hour before applying the contrast material, Prior to CM administration	All patients received 0.9% saline at a rate of 1.0 ml/kg body weight/hour by an infusion pump for 12 hrs prior to and after contrast media administration and continuing for 12 hrs afterward
				2	N-acetylcysteine	IV	600mg, over the course of 30 minutes, at 24 hrs and 1 hour before applying the contrast material, Prior to CM administration	
				3	Ascorbic acid	IV	500mg, over the course of 30 minutes, at 24 hrs and 1 hour before applying the contrast material, Prior to CM administration	
Burns, 2010 [16]	Not specified	NR	Not specified, Not specified	1	Placebo	IV	Placebo NR, 12 hrs prior to procedure and 12 hrs after, Prior to CM administration After CM administration	All patients received normal saline hydration
				2	Nac	IV	10 g NAC, 12 hrs prior to procedure and 12 hrs after, Prior to CM administration After CM administration	All patients received normal saline hydration
Carbonell, 2007 [17]	Iopromide	IA	Not specified, Not specified	1	Placebo	IV Other, placebo	Saline IV for 30 min bid x4doses, 2days, Prior to CM administration After CM administration	Starting 6 hours before CM Saline infusion 6h before-12h after
				2	Nac	IV	NAC 600 mg IV for 30 min bid x4doses, 2days, Prior to CM administration After CM administration	Starting 6 hours before CM
Carbonell, 2010 [18]	Iopromide	IA	Not specified	1	Placebo	IV	Placebo bid, 2 days, Prior to CM administration After CM administration	Saline 0.45% 1ml/kg/h infusion 6h before-12 after
				2	Nac	IV	NAC 600mg bid, 30 min infusion bid - 2 days, Prior to CM administration After CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Castini, 2010[19]	Iodixanol	IA	320mg/ml	1	IV saline	IV	1 ml/kg isotonic saline body weight per hour for 12 hrs before and 12 hrs after administration of the contrast agent	
				2	IV saline + NAC	Oral	600 mg twice daily, NAC, 12 hrs before and 12 hrs after administration of the contrast agent, prior and during CM administration plus IV saline regimen of Arm 1	1 ml/kg body weight per hour for 12 hrs before and 12 hrs after administration of the contrast agent
				3	IV sodium bicarb	IV	154 ml of 1000 meq/L SB added to 846 ml of 5% dextrose in H2O. 3 ml/kg for 1 hour immediately before contrast injection. Thereafter, patients received the same fluid at a rate of 1 ml/kg per hour during contrast exposure and for 6 hrs after the procedure. Prior, during and after CM administration	
Chousterman, 2013 [21]	Iohexol	IA and IV	Not specified, Define, 100 mL (90-120) for NAC vs 90mL (80-120) for without NAC	1	Saline	NR	0.9% saline, Prior to CM administration After CM administration	All patients received saline 0.9% 24h infusion- 12 h before and 12 h after examination
				2	Nac	Oral	NAC 2400mg, 2 days, Prior to CM administration After CM administration	37% of the patients received 600mg pre- 63% received 1200mg. All patients received 2400mg total
Chousterman, 2013[21]	Iohexol	Either IA or IV	Median: 90ml in control, 100ml in NAC group	1	No NAC	NR	Nr	All patients received 0.9% saline hydration for 12 hrs before and 12 hrs after procedure.
				2	Nac	Oral	600mg, twice daily, 2400mg total. 48 hrs. Prior and after cm administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Demir, 2008 [22]	Iomeprol, Iopamidol	IV	100ml: Iomeprol (61.25 g/ml) Iopamidol (61.25 g/ml), Not specified, Define, 100ml: Iomeprol (61.25 g/ml) Iopamidol (61.25 g/ml)	1	Saline	IV	2000ml 0.9% saline hydration, 48 hours (24 pre and 24 post), and after CM administration	
				2	Saline + NAC (NAC)	Oral	Hydration as arm 1 + NAC 600 ml/d, 3 days prior, day of, 1 day post procedure	
				3	Saline + Misoprostol (M)	Oral	Hydration as arm 1 + Misoprostol 400 mg/d (200mg, bid), 3 days prior, day of, 1 day post procedure	
				4	Saline + Theophylline (T)	Oral	Hydration as arm 1 + Theophylline 200mg/d, 3 days prior, day of, 1 day post procedure	
				5	Saline + Nifedipine control (N)		Hydration as arm 1 + Nifedipine 30 mg/day, 3 days prior, day of, 1 day post procedure	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Durham, 2002[23]	Iohexol	IA	Mean: Arm1 48.1 min (SD 30.9), Arm2 44.8 min (SD 19.1), Define, Mean: Arm1 84.7 ml, Arm2 77.4 ml	1	IV hydration plus placebo	Oral	Saline 0.45% 1 ml/kg/h, placebo NR, 1h before and 3h after, Prior to CM administration After CM administration	Saline hydration given for 12 hrs before and and up to 12 hrs after procedure All patients were placed on conventional iv hydration but actual rate and duration was left to physician
				2	IV hydration plus NAC	Oral	Saline 0.45% 1 ml/kg/h, 1200mg NAC, 1h before and 3h after, Prior to CM administration After CM administration	Saline hydration given for 12 hrs before and and up to 12 hrs after procedure
Ferrario, 2009 [24]	Iodixanol	IA	250 mOsm/kg, Not specified	1	Placebo	Oral, IV	NR glucose placebo pills, 2 days, Prior to CM administration During CM administration	IV 0.9% saline given day before procedure and 24 hrs after procedure
				2	Nac	Oral, IV	600mg NAC twice a day, 2 days, Prior to CM administration During CM administration	IV 0.9% saline given day before procedure and 24 hrs after procedure
Frank, 2003[25]	Iomeprol	IA	mean dose was 80 mL; 3 CM injections into LCA and 2 injections into the RCA + biplane levocardiography using 25 mL	1	0.9% saline volume expansion	IV	1000 ml 0.9% saline, 12 hrs. Prior and After CM administration	6 hrs pre and 6 hrs post CM admin
				2	0.9% saline voume expansion + high-flux HD	IV + HD	1000 ml 0.9% saline (same as control)HD high flux started 10 min before CM and continued for 4 hrs during CM admin.	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Fung, 2004 [26]	Iopromide, LOCM, Other description, (iodine, 300 mg/mL; Ultavist; Shering Moldova, Berlin, Germany). Note that only iopromide was used. It is a LOCM, but was the ONLY one used	IA	(iodine, 300 mg/mL), Not specified, Define, Arm 1 mean 121.0 +/- 66.2 mL. Arm 2 mean=135.8 +/- 66.6 mL	1	IV hydration+ No drug	IV	Normal saline at 100 ml/h from 12 hrs before the procedure until 12 hrs after the procedure, unless the patient was in clinical heart failure, 24, Prior to CM administration During CM administration After CM administration	Six patients in NAC and 7 patients in the control group could not complete the saline infusion regimen because of clinical heart failure
				2	IV hydration +NAC	Oral, IV	Oral NAC 400 mg, thrice daily the day before and day of the contrast procedure+ normal saline (at 100 ml/h from 12 hrs before the procedure until 12 hrs after the procedure, unless the patient was in clinical heart failure, NAC x 2 days and NS x 24 hrs, Prior to CM administration After CM administration Other, The NS was also given during CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Goldenberg, 2004[27]	Iopamidol	IA	Boluses of 8-15ml, Not specified, Define, boluses of 8-15ml	1	Placebo plus IV saline 0.45%	Oral	N/A, Prior to CM administration During CM administration After CM administration	All patients were treated with IV saline (0.45%) at a rate of 1 ml/kg of body weight per hour for 12 h before and 12 h after administration of the contrast agent. All patients were treated with IV saline (0.45%) at a rate of 1 ml/kg of body weight per hour for 12 h before and 12 h after administration of the contrast agent.
				2	Acetylcysteine plus IV saline 0.45%	Oral	600mg thrice daily, 48hrs, Prior to CM administration During CM administration After CM administration	All patients were treated with IV saline (0.45%) at a rate of 1 ml/kg of body weight per hour for 12 h before and 12 h after administration of the contrast agent.
Gomes, 2005 [28]	Ioxaglate	IA	Not specified, Define, 102.5 (SD 47.3) ml in NAC group; 102.8 (60.4) ml in placebo group	1	Placebo	Oral	Placebo, starting one day before the procedure (two doses before and two doses after the procedure, Prior to CM administration After CM administration	All patients received IV saline 0.9% 1 ml/kg/h from 12 hours before to 12 hours after exposure to the contrast medium All patients received IV saline 0.9% 1 ml/kg/h from 12 hours before to 12 hours after exposure to the contrast medium
				2	N-acetylcysteine	Oral	600mg bid, starting one day before the procedure (two doses before and two doses after the procedure, Prior to CM administration After CM administration	All patients received IV saline 0.9% 1 ml/kg/h from 12 hours before to 12 hours after exposure to the contrast medium

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN (continued)

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Gomes, 2012 [29]	Ioxaglate	IA	Not specified, Define, Mean: Arm1 125(SD 87), Arm2 124 (SD 65)	1	Saline solution	IV	0.9% saline solution- 3ml/kg/hr x one hour pre and 1ml/kg/hr x 6 hrs post, 7 hrs total, Prior to CM administration After CM administration	
				2	NaHCO3	IV	154 meq/l NaHCO3 in 5% dextrose solution- 3ml/kg/hr x one hour pre and 1ml/kg/hr x 6 hrs post, 7 hrs total, Prior to CM administration After CM administration	
Gulel, 2005 [30]	Ioxaglate	IA	Not specified, Not specified	1	Control	NR		All patients received saline 1ml/kg/h infusion 12 h before-12 h after CM
				2	Nac	Oral	600mg bid, 2days, Prior to CM administration After CM administration	The day before and the day of the day of CM
Gunebakmaz, 2012[31]	Iopromide, LOCm	IA	61-64, Not specified, Not specified	1	Saline	IV	1ml/kg/h, 18 hrs, staring 12 hrs before the procedure, Prior, during and after CM administration	
				2	Saline + Nebivolol	NR	Hydration as arm 1 + Nebivolol 600mg bid, 4 days, starting 2 days before the procedure, Prior, during and after CM administration	
				3	Saline + NAC	IV	Hydration as arm 1 + NAC 5mg day, 4 days, starting 2 days before the procedure, Prior, during and after CM administration	
Han, 2013[32]	Iodixanol	Not specified	Not specified	1	Usual care	IV	Isotonic saline (0.9% sodium chloride, 1 mL/kg/h) started 12 hours before and continued for 24 hours after contrast medium administration. plus	Statin therapy was resumed in both groups 3 days after contrast media administration, following completion of the study endpoints
				2	Rosuvastatin	IV	Usual care plus rosuvastatin 10 mg every evening from 2 days before to 3 days after contrast medium administration (total dose of 50 mg rosuvastatin over 5 days)	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN. (continued)

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Heguilen, 2013 [33]	Ioversal LOCM	IA	NR	2	NaHCO3	IV	154 mmol NaHCO3, at 3ml/kg, 2 hours prior to CM administration and 1 ml/kg for 6-12 hours post CM administration.	NaHCO 3 group received 154 mEq/l of sodium bicarbonate in 5 % dextrose in H 2 O, mixed by adding 77 ml of 1,000 mEq/l sodium bicarbonate to 423 ml of 5 % dextrose in H 2 O
				3	NAC + NaCHO3	Oral, IV	600mg NAC, twice daily., 2 days, Prior to CM administration During CM administration plus 154 mmol NaHCO3, at 3ml/kg, 2 hours prior to CM administration and 1 ml/kg for 6-12 hours post CM administration.	
				4	NAC	Oral, IV	600mg NAC plus 154 mmol NaCl solution at 3ml/kg/h, 2 days, Prior to CM administration During CM administration After CM administration	Saline solution given 2 hrs before procedure and 12 hrs after. NAC given in same schedule as Arm3
Holscher, 2008[34]	Iopromide	NR	Not specified	1	Hydration only	IV	500 ml 5% glucose and 500 ml 0.9% NaCl, 12h before and 12 h after	
				2	Hydration plus dialysis	IV	Hydration same as arm 1 + dialysis	Low-flux HD started within 20 min after procedure. Duration: 2 hours
				3	Hydration plus NAC	Oral, IV	Hydration same as arm 1 + NAC	NAC 600 mg x4 (2 doses before and 2 doses after)

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued)

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Hsu, 2007 [35]	Iohexol, LOCM, Other description, Omnipaque	IA	>1.5ml/kg, Not specified, Define, Mean+/- SD=188.6 +/- 57.9 ml	1	Iv hydration + placebo	Oral, IV	IV 0.45% Saline at rate of 1ml/kg/hr + placebo pills 4 doses total, 2 before procedure and 2 after., 24hrs of IV fluid, 48 hrs of placebo pills, Prior to CM administration After CM administration	Placebo pills looked identical to that containing the NAC but was empty
				2	IV hydration + N-acetylcysteine	Oral, IV	Oral NAC 600mg twice a day. 2 doses before and 2 doses after procedure +IV 0.45% Saline at rate of 1ml/kg/hr 12 hrs before and 12 hrs after procedure, 48h, Prior to CM administration After CM administration	
Hsu, 2012 [36]	Iohexollopromide, Other description, Iobitridol	IV	Iohexol= 350 mgI/L, Iobitridol= 350 mgI/mL, Iopromide= 370 mgI/mL, Not specified	1	Control	IV	0.9% NaCl at 3ml/kg for 60 mins before CECT, then continued at 1 ml/kg/h during and for 6 hrs after procedure. Volume was reduced in patients with congestive pulmonary edema or heart failure, Prior to CM administration During CM administration After CM administration	
				2	Nac	IV	600 mg of NAC in 0.9% NaCl for 60 mins prior to contrast injection, Prior to CM administration	
Izani Wan Mohamed, 2008[37]	Iohexol	IA	Arm 1 mean (SD) = 126.67(94.37)ml Arm 2 mean (SD)=136.73 (100.23)ml	1		IV	Saline (0.45% NS) was given intravenously at a rate of I ml/kg/h 12 hrs before and after coronary angiogram Prior to CM administration After CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Izani Wan Mohamed, 2008[37] (continued)				2		Oral, IV	Oral NAC 600mg twice daily for four doses starting 12 hrs before procedure + Saline (0.45% NS) was given intravenously at a rate of l ml/kg/h 12 hrs before and after coronary angiogram Prior to CM administration After CM administration	
Jaffery, 2012 [38]	Iodixanol, IOCM	NR	Not specified,Define, High dose >300ml received by some. others received less than 300ml	1	Hydration	IV	Not specified, 24 hrs, Not stated,	Volumes infused comparable between groups
				2	Nac	IV	6g total-1200mg bolus then 200mg/hr for 24 hrs, 24 hrs, Not stated,	Saline0.9% infusion 1 ml/kg/hr for 24 hr. Patients with clinical evidence of heart failure (volume overload) received only intravenous NAC
Jo, 2008[39]	IOCM	IA	320mg iodine/ml	1	Placebo	Oral	NR, Prior and After CM administration on the same schedule as those receiving active treatment	All patients received intravenous half-isotonic saline at a rate of 1 mg/kg per hour for 12 hours before and 12 hours after coronary catheterization
				2	Simvastatin	Oral	40mg 12 hourly, 2 days. Prior and after cm administration	
Kay, 2003[40]	Iopamidol	IA	at the discretion of MD, Not specified, Not specified	1	Placebo	Oral	Placebo bid, 2 days, Prior to CM administration After CM administration	All pts received saline 0.9% 1ml/kg/h infusion 12h before-6 h after CM
				2	Nac	Oral	NAC 600mg bid, 2 days, Prior to CM administration After CM administration	
Kefer, 2003 [41]	Iohexol, Iopromide	NR	Not specified, Not specified	1	Placebo	IV	Placebo NR, NR, Prior to CM administration After CM administration	Placebo given 12 hrs prior to procedure, and after procedure (time frame and dose not given)
				2	Nac	IV	2400mg, NR, Prior to CM administration After CM administration	1200mg given 12 hrs prior to procedure, and 1200mg after procedure (time frame not given)

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Khalili, 2006 [42]	Iohexol	NR	647mg, Not specified, Define, 140ml	1	Saline	IV	1000ml normal saline, NS, Prior to CM administration	Saline given at 1ml/kg/h
				2	NAC + saline	IV	1000ml normal saline + 1200mg NAC daily, 2 days, Prior to CM administration During CM administration	NAC given day prior to imaging and day of CM infusion
Kim, 2010[43]	Iodixanol, Iopamidol, Other description, Iobitridol	IA	Define, 39+/-24min for treatment group and 46+/-30 for control group, Define, 201+/-144ml for treatment group and 216+/-166 for control group	1	Control	NR	Not stated	Physiological (0.9%) saline was given intravenously at a rate of 1 ml/kg of body weight per hour for 12 h before and 6 h after coronary angiography in both groups.
				2	Nac	Oral	600mg twice a day, 1200mg total, 48hrs, Prior to CM administration During CM administration	
Kimmel, 2008[44]	Iomeprol	IA	Not specified	1	Placebo	Oral	NR, 48 hrs, Prior to CM administration During CM administration	Day before and day of procedure All patients received a peri-procedural intravenous infusion ('volume expansion') of 1 ml/kg/h with 0.45% saline for 24 h (12 h before and 12 h after exposure to CM)
				2	Nac	Oral	600mg b.i.d, 48 hrs, Prior to CM administration During CM administration	Day before and day of procedure
				3	Zinc	Oral	60mg daily, 24 hrs, Prior to CM administration	Day before
Kinbara, 2010[45]	Iopamidol,	IA	0.755g/ml	1	Hydration	IV	1ml/kg/hr, 30min before and 10hrs after angiography, prior and after CM administration	All arms given normal saline
				2	Hydration and aminophylline	IV	250mg +control treatment, 30min before+control treatment, Prior to CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Kinbara, 2010[45] (contineud)				3	Hydration and N-acetylcysteine	Oral	704mg twice daily+control treatment, day before and during procedure+control, prior and during CM administration	
Koc, 2013 [46]	Not specified	IA	Median: Arm1 90ml, Arm2 90ml, Not specified	1	Normal saline	IV	1 ml.kg.hr 0.9% Saline, 24 hrs, Prior to CM administration After CM administration	12 hrs before and 12 hrs after contrast
				2	NaHCO3	IV	154ml of 1000 meq/l NaHCO3, 12 hrs, Prior to CM administration After CM administration	6 hrs before and 6 hrs after contrast
Kotlyar, 2005[47]	Iopromide, Other description, Ultravist-370, 0.769 mg/ml, 370mg iodine/ml; Schering Berlin, Germany	IA	Not specified, Define, mean 87ml in Arm 1, mean 89 ml in Arm 2 and mean 86ml in Arm 3	1	IV hydration	IV	0.9% saline commenced at 200 ml/h 2 h before angiography and continued for a further 5 h after the procedure, NR, Prior to CM administration After CM administration	All patients, scheduled for angiography, received written instruction to drink 1 l of fluid the evening prior to the procedure
				2	NAC 300mg	Oral	IV NAC 300mg +IV Hydration0.9% saline (Nacl at 200 ml/h 2 h before angiography and continued for a further 5 h after the procedure), NR, Prior to CM administration After CM administration	NAC was prepared in 100 ml of 5% dextrose and administered over 20 min, 1–2 h before angiography and again 2–4 h after angiography
				3	NAC 600mg	Oral	IV NAC 600mg +IV hydration 0.9% saline (NaCl at 200 ml/h 2 h before angiography and continued for a further 5 h after the procedure), NR, Prior to CM administration After CM administration	NAC was prepared in 100 ml of 5% dextrose and administered over 20 min, 1–2 h before angiography and again 2–4 h after angiography

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Lee, 2011 [48]	Iodixanol	IA	Not specified, Define, Mean: Arm1 120ml, Arm2 113ml	1	Saline	IV	0.9% saline, 1 ml/kg/hour, 24 h infusion- 12 h before - 12 h after procedure, Prior to CM administration During CM administration After CM administration	All patients given 1200mg of NAC 2 times a day for 2 days
				2	NaHCO3	IV	154 meq/L 3ml/kg/h before CM-1ml/kg/h after CM, 7 h infusion-1 h before -6 h after, Prior to CM administration During CM administration After CM administration	
Lehnert, 1998 [49]	Iopentol, Other description, the concentration of the iopentol: 350 mg iodine/mL = 810 mOs/kg H2O)	IA and IV	3.0ml/kg(SD=0.4) for control and 3.5 ml/kg(SD=0.6) for the hemodialysis group, Not specified	1	Saline	IV	0.9% saline at 83 ml/hour, 24 hours 12 h before contrast, and 12 hours after contrast	If the patient was not on a calcium channel blocker, then 10 mg nitrendipine per 12 hours was scheduled beginning 12 hours before catheterization
				2	Hemodialysis	Other, Vascular accces shaldon catheter (femoral vein)	Hydrations as arm1 High flux hemodialysis at a flow 500 ml/min. for 3 hours started started 63+/- min after last bolus of CM	If the patient was not on a calcium channel blocker, then 10 mg nitrendipine per 12 hours was scheduled beginning 12 hours before catheterization.

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Li, 2012 [50]	Ultravist 370, iodine 370 mg/ml	NR	NS	1	Control	Oral, IV	Placebo 80 mg p.o before procedure; IV isotonic saline (0.9%) at a rate of 1 ml/kg/h before the procedure and for 12 h after the procedure, Prior to CM administration After CM administration	after procedure all patients had long term torvastatin treatment 40 mg/day. Iv isotonic saline (0.9%) at a rate of 1 ml/kg/h before the procedure and for 12 h after the procedure, prior to cm administration after cm administration
				2	Atorvastatin	Oral, IV	Atorvastatin load 80 mg p.o before procedure,	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
MacNeill, 2003 [51]	Iopromide, Ioxilan	IA	Not specified, Define, mean 110(sd=57.7)ml overall; 116 +/- 63.3 mL in placebo group and 103 +/- 52.0 in placebo group	1	Placebo	Oral, IV	Oral placebo (same schedule as in Arm 2) + IV 0.45% saline: 1. Pre-treatment: 1 ml/kg/hr x 12 hrs for inpatients and 2 ml/kg/hr x 4 hrs for day-case patients. Postprocedure: all patients were given 0.45% saline at 75 ml/hr x 12 hrs, oral placebo (same schedule as in Arm 2). IV saline: inpatients: total duration of 24 hrs. Day-case patients: 16 hrs total, Prior to CM administration After CM administration	All patients were pretreated with 0.45% saline at a rate of 1 ml/kg/hr for 12 hr for in-patients and 2 ml/kg/hr for 4 hr for day-case patients. See above regarding post-procedural fluids
				2	Nac	Oral, IV	600mg oral NAC at time of randomization, then 4 hrs later (pre-catherization), then 3 additional doses after the procedure at 12-hour intervals + control regimen of IVF, same IV schedule as control; NAC: as above (at least 4 hrs pre-procedure, then for at least 24 hrs post-procedure (after procedure, then 12 hrs later, then 12 hrs later), Prior to CM administration After CM administration	
Marenzi, 2003[52]	Iopentol	IA	Not specified	1	Isotonic saline	IV	Saline 0.9% 1ml/kg/h for 24-32 hours (4-8 hours before-18-24 hours after)	Dose was 0.5 ml/kg/hr if ejection fration was less than 40%
				2	Hemofiltration therapy	Continuous venovenous hemofiltration	Hydration as arm 1 + HF started 4-6 h before CM, stopped during procedure and resumed after completion, for 18-24 hours at a flow of 1000 ml/h	Participants received heparin at the start of and during the hemofiltration.

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Marenzi, 2006 [53]	Iohexol, LOCM, Other description, 350 mg of iodine per milliliter; Omnipaque, Amersham Health	NR	Define, Arm 1 mean 274;Arm 2mean= 264;Arm 3 mean= 253	1	Placebo	Other, ns		All treated patients and control patients underwent hydration with intravenous isotonic saline (0.9 percent) at a rate of 1 ml per kilogram of body weight per hour (or 0.5 ml per kilogram per hour in cases of overt heart failure) for 12 hrs
				2	Standard dose NAC	Oral, IV	Total dose of 3000mg, Prior to CM administration After CM administration	Intravenous bolus of 600 mg of N-acetylcysteine before primary angioplasty and a 600-mg tablet orally twice daily for the 48 hrs after intervention
				3	High dose NAC		Total dose of 6000mg, Prior to CM administration After CM administration	Intravenous bolus of 1200 mg of N-acetylcysteine before intervention and 1200 mg orally twice daily for the 48 hrs after intervention
Marenzi, 2006[54]	LOCM	Not specified	Not specified	1	Isotonic saline	IV	Saline 0.9% 1ml/kg/h for 24 hours (12 hours before-12 hours after)	
				2	Isotonic saline plus hemofiltration after contrast exposure	NR	Hydration as arm 1 + HF for 18-24 hours after CM at a flow of 1000 ml/h	
				3	Isotonic saline plus hemofiltration before and after contrast exposure	NR	Hydration as arm 1 + HF started 4-6 h before CM, stopped during procedure and resumed after completion, for 18-24 hours at a flow of 1000 ml/h	
Masuda, 2007[55]	Not specified	Not specified	Not specified	1	NaCl	IV	3ml/kg/hr before and 1ml/kg/hr during and after the procedure, 1hr, 6hrs, Prior, during and after CM administration	Only reports saline as NaCl
				2	NaHCO3	IV	3ml/kg/hr before and 1ml/kg/hr during and after the procedure, 1hr, 6hrs, Prior, during and after CM administration	Only reports saline as NaCl

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Matejka, 2010 [56]	Iodixanol	IA	NS	1	Placebo	IV	IV infusion normal saline before CM - fluids 3days after CM, Prior to CM administration After CM administration	All pts had unrestricted oral fluids before and after the procedure
				2	Theophylline	IV	205.7mg, Theoph-1h infusion before CM in 500 ml normal saline- fluids 3days after CM, Prior to CM administration After CM administration	
Merten, 2004[57]	Iopamidol	NR	796 mOsm/kgH2O, 755mgof iopamidol per milliliter, and 370 mg iodine per milliliter	1	NaCl	IV	3ml/kg per hour for 1 hour before then 1ml/kg per hour during the contrast exposure and for 6 hrs after the procedure, Prior, during and after CM administration	5% dextrose given in all arms
				2	NaHCO3	IV	3ml/kg per hour for 1 hour before then 1ml/kg per hour during the contrast exposure and for 6 hrs after the procedure. Prior, during and after CM administration	5% dextrose given in all arms
Miner,2004 [58]	Iohexol	IA	Not specified, Define, Arm 1 mean=350ml; Arm 2 mean=344ml	1	Placebo	Oral	NS, one dose every 12 hrs, 24 hrs, Prior to CM administration During CM administration	All patients received intravenous hydration with 0.45% saline at 75 ml/hour for at least 24 hrs beginning at the time of enrollment
				2	Nac	Oral	2000mg/dose x 2-3 doses. Total: 4000-6000mg, one dose every 12 hrs, 24 hrs, prior to cm administration during cm administration	Prior day patients received their first dose at 8 pm the night before their procedure with subsequent doses at 8 am and 8 pm the day of their procedure. Same day patients received their first dose at 8 am the day of their pci procedure with a subsequent dose at 8 pm the same day. Thus, if randomized to nac, prior day patients received a total of 6000 mg of nac while same day patients received a total of 4000 mg.

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Motohiro, 2011[59]	Iopamidol, LOCM	IA	Not specified	1	Nacl	IV	1ml/kg/hr of NaCl, 12 hr before and after, Prior, during and after CM administration	Total infusion 24 h - 12h before/12 h after with saline
				2	Bicarbonate	IV	1ml/kg/h (154 meq), 9h - 3 h before-/ 6 h after, Prior, during and after CM administration	
Ochoa, 2004 [60]	Iodixanol, Iohexol, Ioxaglate, Other description, diatrizoate	IA	151 +/-71 mL(placebo group) and 136 +/-78 mL (NAC group), Not specified, Define, Arm 1 mean+/-SD=151 +/-71 mL and Arm 2=136 +/-78 mL	1	Placebo	Oral	5ml 0.9% saline diluted in 20 ml diet cola, 1 hr prior and 4 hr after, Prior to CM administration After CM administration	Saline IV 150 ml/h starting 4hr before and continuing 6 hr after procedure
				2	Nac	Oral	2 doses of NAC (1000 mg (5ml) in 20 ml diet cola, 1 hr prior and 4 hr after, Prior to CM administration After CM administration	Saline IV 150 ml/h starting 4hr before-and continuing 6 hr after procedure
Oldemeyer, 2003[61]	Iopamidol	IA	Not specified, Define, Mean: Arm1 127ml (sd 73), Arm2 134ml (SD 71)	1	Placebo	Oral	Placebo in 120 ml bev every 12 h/ 4 doses, 2 days, Prior to CM administration After CM administration	Starting the night before CM All pats received saline 0.45% 1ml/kl/h infusion 12h before-12h after CM
				2	Nac	Oral	NAC 1500 mg diluted in 120ml bev - every 12 h/4 doses, 2 days, Prior to CM administration After CM administration	Starting the night before CM
				3	Saline + NAC	Oral, IV	1ml/kg/h + NAC 600 mg bid starting the day before CM, 12 h inf (6 h before -6 h after), Prior to CM administration During CM administration After CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Ozcan, 2007[62]	Ioxaglate LOCM	IA	Median: 110 ml (25-300), Not specified, Define, comparable between groups	1	Saline	IV	1ml/kg/h, 12 h inf (6 h before -6 h after), Prior to CM administration During CM administration After CM administration	154 meq
				2	NAC + saline	Oral, IV	600mg oraly wice daily day before and day of procedure plus saline protocol in Arm 1	154meq
				3	Sodium bicarbonate + Saline	IV	154 mL of 1000-mEq/L sodium bicarbonate to 846 mL of 5% dextrose in water plus saline protocol in Arm 1	
Ozhan, 2010[63]	Iopamidol	IA	Not specified, Define, comparable between groups	1	Nac	Oral	NAC 600 mg twice daily, day after procedure, 1 day, After CM administration	Saline 1000 ml infusion for 6 h after procedure
				2	Nac + atorvastatin	Oral	NAC 600 mg and Atorvastatin 80 mg twice daily on day 1 after procedure. Atorvastatin 80mg d for 2 days after procedure, 3 days, After CM administration	Saline 1000 ml infusion for 6 h after procedure
Patti, 2011 [64]	Iobitridol	IA	915 mOsm/kg, Not specified, Define, Mean: Arm1 213ml (SD 13), Arm2 209ml (SD72)	1	Placebo	Oral	Placebo, not specified, first dose 12 hrs before and another dose 2 hrs before procedure, Prior to CM administration	All patients received 40mg/day of atorvastatin after PCI.
				2	Atorvastatin	Oral	Total 120mg (80mg and 40mg doses), 80mg 12 hrs before procedure and 40mg 2 hrs before procedure, Prior to CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Poletti, 2007[65]	Iopromide	IV	A bolus of 2 mL/kg body weight was used for nonneurologic indications, and a standard dose of 100 mL was used for brain imaging or suspicion of pulmonary embolism, Not specified, Define, A bolus of 2 mL/kg body weight was used for nonneurologic indications, and a standard dose of 100 mL was used for brain imaging or suspicion of pulmonary embolism	1	Hydration plus placebo	IV	N/A, 1hr before and up to 12hrs after, Prior to CM administration After CM administration	Each patient was assigned to receive 0.45% saline solution IV at a rate of 5 ml/kg body weight over the course of the hour before CT and followed at a rate of 1 ml/kg body weight for 12 hrs after CT. Each patient was assigned to receive 0.45% saline solution IV at a rate of 5 ml/kg body weight over the course of the hour before CT and followed at a rate of 1 ml/kg body weight for 12 hrs after CT.
				2	Hydration plu N-acetylcysteine	IV	900mg before and 900mg after, 1hr before and up to 12hrs after, Prior to CM administration After CM administration	Each patient was assigned to receive 0.45% saline solution IV at a rate of 5 ml/kg body weight over the course of the hour before CT and followed at a rate of 1 ml/kg body weight for 12 hrs after CT.
Quintavalle,2012 [66]	Iodixanol	IA	Not specified	1	Control	NR	Only CKD prophylaxisis	All patients received CKD prophylaxisis : NAC 1200 mg orally twice daily the day before and day of administration of contast and NaHCO3 (154 meq/L in dextrose and H2O), 3 ml/kg/hr 1 hour before and 1 ml/kg/hr for 6 hrs after contrast
				2	Atorvastatin	Not reported,	80mg, within 24 hrs of procedure, Prior to CM administration	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Ratcliffe, 2009 [67]	Iodixanol, IOCM	IA	Was not standardized due to variation among patients	1	Saline alone	IV	Normal saline (0.9% saline in 5% dextrose) at an infusion rate of 3 ml/kg/h for 1 h before contrast, and continued at 1 ml/kg/h during the procedure and for 6 h following contrast exposure.	
				2	NAC + Saline	Oral, IV	IV bolus of 1200 mg of NAC 1 h before intervention and 1200 mg orally twice daily for 48 h after intervention + IV NaCl (154 meq/L NaCl in 5% dextrose), at an infusion rate of 3 ml/kg/h for 1 h before contrast, and continued at 1 ml/kg/h during the procedure and for 6 h following contrast exposure, with normal saline as Arm 1	
				3	NaHCO3 alone	IV	IV NaHCO3 (154 ml of 1000 meq/L NaHCO3 to 846 ml of 5% dextrose, slightly diluting the dextrose concentration to 4.23%) at an infusion rate of 3 ml/kg/h for 1 h before contrast, and continued at 1 ml/kg/h during the procedure and for 6 h following contrast exposure..	
				4	NaHCO3 plus NAC	Oral, IV	IV bolus of 1200 mg of NAC 1 h before intervention and 1200 mg orally twice daily for 48 h after intervention + NaHCO3 (154 ml of 1000 meq/L NaHCO3 to 846 ml of 5% dextrose, slightly diluting the dextrose concentration to 4.23%) at an infusion rate of 3 ml/kg/h for 1 h before contrast, and continued at 1 ml/kg/h during the procedure and for 6 h following contrast exposure.	

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Reinecke, 2007 [68]	Iopromide, IOCM, Other description, (Ultravist 370TM, Schering AG, Berlin, Germany).	NR	Arm1:mean 188; Arm 2 mean184; Arm3 mean197mg/dl, Not specified	1	Hydration only	IV	Glucose 5% + Saline 0.9% 24 h (2000 ml 12 h before- 12 h after CM	
				2	Hydration + dialysis	IV, Other, hemodialysis	Hydration as arm 1 + Low-flux HD started within 20 min after procedure. Duration: 2 hours	
				3	Hydration + NAC	Oral, IV	Hydration as arm 1 + NAC 600 mg x4 (2 doses before and after)	One dose NAC 600 mg was given at the evening before catheterization, the second dose was given on the morning before catheterization; the third was given at the evening after catheterization and the last dose was given on the morning the day after angiography.

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Sadat, 2011[69]	Iopamidol	IA	Not specified	1	IV Hydration only	IV	1 L iv infusion over a period of 12 hrs before angiography and 1 L over 12 hrs following the procedure)., 24 hrs, Prior to CM administration After CM administration	12h before and 12h after
				2	Hydration+NAC	Oral	Oral NAC 600 mg twice daily the day before the angiogram and 600 mg twice on the day of the angiogram along with iv fluids, 48 hrs, Prior to CM administration During CM administration After CM administration	Day before and day of procedure
Sandhu, 2006 [70]	Iodixanol, Iopamidol	IA	Not specified, Define, 150.9 ml +/- 78.6 in NAC group, 125.4 +/- 67.4 ml in control group	1	Control	Not reported		They do not specify if NAC is oral , Hydration not part of protocol, left up to physician
				2	Nac	Not reported	NAC 600mg bid, the day before and the day of the procedure, Prior to CM administration	They do not specify if NAC is oral , Hydration not part of protocol, left up to physician
Seyon, 2007[71]	Iohexol	IA	147.5+/- 74.5 ml (tc); 133.68+/-58.04 (control)	1	Placebo+hydration	Oral	Placebo similar to NAC, once before procedure and then twice daily after for total of 4 doses. Prior and After CM administration	IV saline 0.45% 1 ml/kg/hr; 4-6 hrs pre and 12 hrs post
				2	N-Acetylcysteine+hydration	Oral	600mg, once before procedure and then twicw daily after for total of 4 doses. Prior and after cm administration	Iv saline 0.45% 1 ml/kg/hr; 4-6 hrs pre and 12 hrs post

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN. .(continued)

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Shavit, 2009 [72]	Iopamidol LOCM	NR	755 mg iopamidol per milliliter, and 370 mg iodine per milliliter, Not specified	1	NaHCO3	IV	154 mq/L NaHCO3 in 5% dextrose. The initial IV bolus was 3 ml/kg for 1 hour before cardiac catheterization. Following this bolus, patients received the same fluid at a rate of 1 ml/kg per hour during the contrast exposure and for 6 hrs after the procedure, .	
				2	NAC+NaCl	Oral, IV	NAC 600 mg× 2/d PO the day before and the day of the procedure., 2d, Prior to CM administration plus sodium chloride at 1 ml/kg/hr for 12 hours prior to infusion	
Shyu, 2002 [73]	Iopamidol LOCM	NR	0.755mg/ml, Not specified	1	NAC + 0.45% saline	Oral, IV	Placebo, placebo, Prior to CM administration After CM administration	Placebo + 0.45% saline, saline given 12 hrs before and 12 hrs after procedure
				2	0	Oral, IV	400mg, twice a day, 2 days, Prior to CM administration During CM administration After CM administration	NAC given orally day before procedure and day of procedure. 0.45% saline given by IV. Saline given 12 hrs before and 12 hrs after procedure
Tanaka, 2011[74]	Iopamidol, LOCM	IA	755mg/ml, range 205-216 +/- 80	1	Placebo	Oral	4 ml of water	Ringer lactate 1-2 ml/kg/h for 12 hr after pci Volume of cm given per arm, comparable, dose not specified
				2	Nac	Oral	705 mg every 12 h/ total 2820, 36 hrs	Ringer lactate 1-2 ml/kg/h for 12 hr after pci

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Tepel, 2000 [75]	Iopromide	IV	75 mL of .623g /mL with 300mg/mL iodine, Not specified, Define, • 75 mL of .623g /mL with 300mg/mL iodine	1	Not in PC Tables	IV	Placebo-N/A, Saline 1ml/kg 12 hrs before and 12 hrs after administration, 24 hrs, Prior to CM administration During CM administration After CM administration	
				2	Not in PC Tables	Oral, IV	Acetylcysteine 600mg orally twice daily before and on day of contrast administration, Saline 1ml/kg 12 hrs before and 12 hrs after administration, 2days, Prior to CM administration During CM administration After CM administration	Plus placebo
				3	Not in PC Tables			
				4	Not in PC Tables			
Thiele, 2010[76]	Iopromide	IA	Not specified, Define, median=180 ml	1	Placebo	IV	10ml of NaCl 0.9% before angio, 10 mls twice daily for 48h after PCI, 48 hrs, Prior to CM administration After CM administration	After PCI, all treated and control patients underwent hydration with intravenous NaCl (0.9%) infusion at a rate of 1ml/kg of body weight per h for 12 h (or 0.5ml/kg/h in overt heart failure)
				2	Nac	IV	1,200mg twice daily, 6000mg, 48 hrs, Prior to CM administration After CM administration	IV bolus of 1,200 mg before angioplasty and 1,200 mg intravenously twice daily for the 48 h after PCI (total dose 6,000 mg
Toso, 2010[77]	Iodixanol	IA	Not specified	1	Placebo	Oral	Placebo NR, 4 days - starting 48 h before CM-48 h after, Prior to CM administration After CM administration	Saline 1ml/kg/h infusion 12h before CM-12 after + NAC VO 1200mg bid 1 day before CM and day after
				2	Atorvastatin	Oral	Atorvastatin 80mg/d, 4 days - starting 48 h before CM-48 h after, Prior to CM administration After CM administration	Saline 1ml/kg/h infusion 12h before CM-12 after + NAC VO 1200mg bid 1 day before CM and day after

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Ueda, 2011[78]	Iohexol, Iopamidol,	IA	Not specified	1	NaCl	IV	0.5 ml/Kg bolus, Prior, during and after CM administration	Followed by infusion at 1ml/kg/h for 6 hr Volumes were comparable. Given at the discretion of MD
				2	NaHCO3	IV	154 meq/L bolus, Prior, during and after CM administration	
Vasheghani-Farahani, 2010 [79]	Iohexol	IA	Not specified, Define, 123 arm 1- 112 arm 2	1	Saline	IV	Saline 0.45% - 1075ml, 7h infusion (1 h prior- 6h after), Prior to CM administration During CM administration After CM administration	Infusion- 3ml/kg/h prior CM then 1ml/kg/h
				2	Bicarbonate	IV	Saline 0.45% 1000ml + 75ml 8.4% bicarbonate, 7h infusion (1 h prior- 6h after), Prior to CM administration During CM administration After CM administration	Infusion- 3ml/kg/h prior CM then 1ml/kg/h
Vogt, 2001[80]	LOCM	Not specified	Not specified	1	IV saline	IV	1 ml/kg/hr, 24 hrs (12 hrs before and after contrast administration)	
				2	IV saline/Hemodialysis	IV, hemodialysis	Hydration as arm 1 + High-flux HD started between 30 and 280 min after first bolus of CM Duration: 3 hours	Hd: high-flux polysulphone membrane (f50 or f60)). The mean blood flow was 180

Evidence Table 3. Interventions for studies comparing interventions to prevent development of CIN.(continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Webb, 2004 [81]	Other description, Ioversol	IA	Not specified, Define, Median 120 ml in both groups	1	Placebo	IV	50ml of 5% dextrose saline, 15 minutes, Prior to CM administration	Placebo Study solution was administered within 15 minutes 1 hrs prior to contrast procedure. According to abstract but not in text, all patients received 200 ml NS prior to procedure and 1.5 ml/kg/h for 6 hr after procedure
				2	Nac	IV	50ml of 5% dextrose saline + 500mg NAC, 15 minutes, Prior to CM administration	NAC mixed into saline and given intravenously
XinWei, 2009[82]	Iodixanol (in patients with CKD) Iohexol (all other patients)	IA	Body weight (kg) x 5ml/SrCr.	1	Simvastatin 20	Oral	20mg/day from admission to the day before PCI, and then resumed simvastatin 20 mg/day for the following days, Up to 48hrs after procedure. Prior and After CM administration	All patients were hydrated with intravenous isotonic saline (0.9%) at a rate of 1 ml/kg body weight per hour for 6 to 12 hrs before and 12 hrs after coronary catheterization to achieve a urinary flow rate of ≥150 ml/hour within 6 hours after PCI.
				2	Simvastatin 80	Oral	80mg/day from admission to the day before PCI, and then resumed simvastatin 20 mg/day for the following days. Up to 48hrs after procedure. Prior and After CM administration	

ACEI= Angiotensin Converting Enzyme Inhibitor, ANP=Atrial Natriuretic Peptide, AVH= Amlodipine Valsartan Hydration, b.i.d=Bi-daily, Bev=Beverage, CAG=Coronary Angiogram, Cc/hr= cubic centimeter per kilogram, CECT=Contrast Enhanced Computed Tomography, CM=Contrast Media, H=Hour, HD=Hemodialysis, hrs=hrs, IA=Intrarterial, IOCM=Iso-Osmolar Contrast Media, IQR=Interquartile Range, IV=Intravenous, IVF=Intrvenous Fluid, LCA=Left Coronary Artery, LOCM=Low-Osmolar Contrast Media, Mcg/kg/min=microgram per kilogram per min, MD= Doctor of Medicine, mEq/l= milliequivalents per liter, Mg/dl=milligram per deciliter, Mg/kg/hour=milligram per kilogram per hour, Mg/kg=milligram per kilogram, Mg=milligram, mls=milliliters, mOsm/kg= milliosmoles per kilogram, N/A=Not Applicable, NAC=N-acetylcysteine, NaCl=Sodium Chloride, NaHCO3=Sodium Bicarbonate, NR=Not Reported, NS=Normal Saline, Osm=Omsolarity, p.o.=By Mouth, PCI=Percutaneous Coronary Intervention, PCWP=Pulmonary Capillary Wedge Pressure, POBID=By mouth twice daily, RCA=Right Coronary Artery, SB=Sodium Bicarbonate, SD=Standard Deviation, Ug/kg/min=microgram per kilogram per minute, VO=Vocal Order

Evidence Table 4. Summary of studies comparing N-acetylcysteine versus IV saline with or without placebo for the prevention of contrast induced nephropathy and other outcomes

Author, year	Comparison	N	Population	Age, range of mean §	No. female (%)‡	Mean follow up	CM Route*	NAC route	Definition of CIN*	Study limitations †
ACT, 2011[1]	Placebo+ NS vs. NAC+ NS	2308	Cr <176umo/L, with PCI	68	892 (39)	30 days	LOCM, IOCM, HOCM IA	Oral	A1	L
Alioglu, 2013[2]	0.45% saline vs. NAC + 0.45% saline	113	General	63-61	38 (34)	48 hours	LOCM (Iomeprol) IA	Oral	A1	H
Allaqaband, 2002[3]	0.45% saline vs. NAC + 0.45% saline	123	Cr >1.6mg/dl, or CrCl <60ml/min	70-71	52 (42)	48 hours	LOCM, IOCM IA	Oral	A2	M
Amini, 2009[4]	Placebo+ NS vs. NAC+ NS	90	CKD	63-65	36 (40)	48 hours	LOCM, IOCM IA	Oral	A3	M
Aslanger, 2012[5]	Placebo + NS vs. high-dose NAC + NS	312	STEMI	56	71 (23)	72 hours	LOCM (Ioxaglate) IA	IV	A1	M
Awal, 2011[6]	NS vs. NAC+ NS	100	Cr ≥1.2mg/dl	52-58	18 (18)	24 hours	NR IA	Oral	A3	H
Azmus, 2005[7]	Placebo + NS vs. NAC + NS	397	Cr >1.3mg/dl, diabetes, or >70 years	66	163 (41)	48 hours	LOCM (Ioversol, Iohexol, Iopamidol), HOCM (diatrizoate) IA	Oral	A3	L
Baker, 2003[8]	NS vs. NAC+ NS	80	Cr >1.36mg/dl or CrCl <50ml/min	67	10 (13)	96 hours	IOCM (Iodixanol) IA	Oral	A1	M
Baskurt, 2009[9]	NS vs. NAC+ NS	217	Moderate CKD	67	87 (40)	12 months	LOCM (Ioversol) IA	Oral	A2	H
Boccalandro, 2003[11]	Placebo + 0.45% saline vs. NAC + 0.45% saline	179	Cr >1.2 mg/dl or CrCl <50ml/min	66	71 (40)	48 hours	IOCM (Iodixanol) IA	Oral	A2	H
Briguori, 2002[14]	0.45% saline vs. NAC + 0.45% saline	183	Cr >1.2mg/dl, CrCL <70ml/min	55-73	25 (14)	5 days	LOCM (Iopromide) IA	Oral	A1	M
Brueck, 2013[15]	Placebo+ NS vs. IV-NAC+ NS vs. IA-NAC+ NS	499	Cr concentration of ≥1.3 mg/dL	69-79	144 (29)	72 hours	LOCM (Iopromide) IA	IV	A2	L
Burns, 2010[16]	Placebo + NS vs. NAC + NS	42	General	NR	NR	5 days	NR, NR	IV	A2	M
Carbonell, 2007[17]	Placebo + 0.45% saline vs. NAC + 0.45% saline	216	General	50-78	51 (24)	48 hours	LOCM (Iopromide) IA	IV	A3	L

Evidence Table 4. Summary of studies comparing N-acetylcysteine versus placebo or usual care for the prevention of contrast induced nephropathy and other outcomes (continued)

Author, year	Comparison	N	Population	Age, range of mean §	No. female (%)‡	Mean follow up	CM Route*	NAC route	Definition of CIN*	Study limitations †
Carbonell, 2010[18]	Placebo + 0.45% saline vs. NAC + 0.45% saline	81	Cr >1.4 mg/dL	69-70	16 (20)	2 days	LOCM (Iopromide) IA	IV	A3	L
Castini, 2010[19]	NS vs. NAC+ NS	156	Cr >1.2 mg/dl	63-81	19 (12)	5 days	IOCM (Iodixanol) IA	Oral	A1	M
Chousterman, 2011 [20]	NS vs. NAC + NS	116	General	47-73	NR	72 hours	LOCM (Iohexol) IA or IV	Oral	A3	H
Chousterman, 2013[21]	NS vs. NAC + NS	140	ICU patients	47-73	NR	72 hours	LOCM (Iohexol) IA or IV	Oral	A3	H
Demir, 2008[22]	NS vs. NAC+ NS	97	General	56-62	43 (44)	3 days	LOCM (Iomeprol, Iopamidol) IV	Oral	A3	H
Durham, 2002[23]	0.45% Saline vs. high-dose NAC + 0.45% saline	79	Baseline Cr >1.7 mg/dL	69-71	27 (34)	144 hours	LOCM (Iohexol) IA	Oral	A2	M
Ferrario, 2009[24]	Placebo+ NS vs. NAC+ NS	200	Moderate to severe chronic renal failure	75	70 (35)	3 days	IOCM (Iodixanol) IA	Oral	A3	M
Fung, 2004[26]	NS vs. NAC + NS	91	Moderate to severe renal impairment	68	27 (30)	48 hours	LOCM (Iopromide) IA	Oral	A3	M
Goldenberg, 2004[27]	Placebo + 0.45% saline vs. NAC + 0.45% saline	80	Chronic renal insufficiency	69-71	14 (18)	7 days	LOCM (Iopamidol) IA	Oral	A1	L
Gomes, 2005[28]	Placebo + NS vs. NAC + NS	156	High risk for CIN	64-67	64 (41)	48 hours	LOCM (Ioxaglate) IA	Oral	A2	L
Gulel, 2005[30]	NS vs. NAC + NS	50	Cr >1.3	49-73	13 (26)	48 hours	LOCM (Ioxaglate) IA	Oral	A2	M
Gunebakmaz, 2012[31]	Saline + NS vs. NAC + NS	120	Cr >1.2 mg/dl	64 -66	37 (31)	5 days	LOCM (Iopromide) IA	NR	A3	H
Holscher, 2008[34]	NS + glucose vs. NAC +NS + glucose	412	General	67-71	136 (33)	30 days	LOCM (Iopromide) IA	Oral	A2	H
Hsu, 2007[35]	NS vs. NAC+ NS	20	Cr ≥1.6mg/dl or eGFR <40ml/mi, diabetic patients	44-84	10 (50)	5 days	LOCM (Iohexol) IA	Oral	A3	M

Evidence Table 4. Summary of studies comparing N-acetylcysteine versus placebo or usual care for the prevention of contrast induced nephropathy and other outcomes (continued)

Author, year	Comparison	N	Population	Age, range of mean §	No. female (%)‡	Mean follow up	CM Route*	NAC route	Definition of CIN*	Study limitations †
Hsu, 2012[36]	NS vs. NAC+ NS	240	General	80	53 (22)	72 hours	LOCM (Iohexol, Iobitridol, Iopromide) IV	IV	A2	H
Izani Wan Mohamed, 2008[37]	0.45% saline vs. NAC + 0.45% saline	100	Renal impairment	56-58	16 (16)	48 hours	LOCM (Iohexol) IA	Oral	A3	L
Jaffery, 2012[38]	Hydration + NS vs. high-dose NAC + NS	398	Myocardial infarction (MI)†	66	146 (37)	72 hours	IOCM (Iodixanol) IV	IV	A1	H
Kay, 2003[40]	Placebo + NS vs. NAC + NS	200	Cr >1.2mg/dl- CrCl <60ml/min	69	77 (39)	7 days	LOCM (Iopamidol) IA	Oral	A1	M
Kefer, 2003[41]	Placebo + dextrose vs. high-dose NAC + dextrose	104	General	61	24 (23)	24 hours	LOCM (Iohexol, Iopromide) IA	IV	A3	L
Khalili, 2006[42]	NS vs. NAC+ NS	70	Cr >1.2mg/dl- CrCl <60ml/min	74	28 (40)	72 hours	LOCM (Iohexol) IA	Oral	A1	H
Kim, 2010[43]	NS vs. NAC + NS	166	Cr >1.5mg/dl	62	66 (40)	48 hours	IOCM (Iodixanol), LOCM (Iopamidol) IA	Oral	A3	M
Kimmel, 2008[44]	Placebo + 0.45% saline vs. NAC + 0.45% saline	54	Cr >1.2mg/dl- CrCl <50ml/min	66-71	14 (26)	2 days	LOCM (Iomeprol) IA	Oral	A2	M
Kinbara, 2010[45]	NS vs. high-dose NAC + NS	45	Stable coronary artery disease	70-71	17 (38)	48 hours	LOCM (Iopamidol) IA	Oral	A2	M
Kotlyar, 2005[47]	NS vs. NAC + NS	60	Cr concentrations ≥0.13 mmol/l	66-69	10 (33)	30 days	LOCM (Iopromide) IA	IV	A2	M
MacNeill, 2003[51]	Placebo + NS vs. NAC + NS	43	Cr ≥1.5 mg/dl at morning of procedure	62-82	6 (14)	72 hours	LOCM (Iopromide, Ioxilan) IA	Oral	A1	H
Marenzi, 2006[53]	Placebo + NS vs. standard-dose NAC + NS vs. high-dose NAC + NS	354	Acute MI, STEMI	62-63	50 (14)	72 hours	LOCM (Iohexol) IA	IV/ Oral	A1	M
Miner, 2004[58]	Placebo + 0.45% saline vs. high-dose NAC + 0.45% saline	180	Moderate renal impairment	69-71	59 (33)	6 months	LOCM (Iohexol) IA	Oral	A1	H

Evidence Table 4. Summary of studies comparing N-acetylcysteine versus placebo or usual care for the prevention of contrast induced nephropathy and other outcomes (continued)

Author, year	Comparison	N	Population	Age, range of mean §	No. female (%)‡	Mean follow up	CM Route*	NAC route	Definition of CIN*	Study limitations †
Ochoa, 2004 [60]	Placebo + NS vs. high-dose NAC + NS	80	Documented chronic renal	70-73	46 (58)	30 days	IOCM (Iodixanol), LOCM (Iohexol), HOCM (Ioxaglate) IA	Oral	A3	H
Oldemeyer, 2003[61]	Placebo + 0.45% saline vs. high-dose NAC + 0.45% saline	96	CrCl <50ml/min, or Cr >1.2 mg/dl	67-86	43 (45)	48 hours	LOCM (Iopamidol) IA	Oral	A3	M
Ozcan, 2007[62]	NS vs. NAC + NS	264	General	69	(25)	2 days	LOCM (Ioxaglate) IA	Oral	A3	L
Poletti, 2007[65]	Hydration + 0.45% saline vs. high-dose NAC + 0.45% saline	100	Cr concentration >106 µmol/L (1.2 mg/dL)	70-73	32 (32)	4 days	LOCM (Iopromide) IV	IV	≥50% increase from CR baseline	L
Ratcliffe, 2009[67]	Saline + NS + dextrose vs. high-dose NAC + NS + dextrose	78	Cr >132.6umo/L or CrCl <1.0ml/s, diabetic	64-67	24 (31)	7 days	IOCM (Iodixanol) IA	IV	A1	H
Reinecke, 2007 [68]	NS vs. NAC + NS + glucose	424	Cr >1.3 mg/dl	67-68	73 (17)	553 days	LOCM (Iopromide) IA	Oral	A2	H
Sadat, 2011[69]	NS vs. NAC + NS	40	Cr >1.2 mg/dl or CrCl <60ml/min	75	NR	7 days	LOCM (Iopamidol) IA	Oral	A1	M
Sandhu, 2006[70]	Usual care (no NAC) vs. NAC (hydration NR)	106	General	66-70	40 (38)	48 hours	IOCM (Iodixanol), LOCM (Iopamidol) IA	Oral	A2	M
Seyon, 2007[71]	Placebo + 0.45% saline vs. NAC + 0.45% saline	40	Renal dysfunction	75-76	14 (35)	48 hours	Most LOCM, one ICOM, one unknown IA	Oral	A2	H
Shyu, 2002[73]	0.45% saline vs. NAC + 0.45% saline	121	Chronic renal failure with stable Cr concentrations	70	39 (32)	7 days	LOCM (Iopamidol) IA	Oral	A2	L
Tanaka, 2011[74]	Placebo + Ringer's Lactate vs. high-dose NAC + Ringer's Lactate	82	STEMI with PCI	61-63	14 (17)	72 hours	LOCM (Iopamidol) IA	Oral	A1	H

Evidence Table 4. Summary of studies comparing N-acetylcysteine versus placebo or usual care for the prevention of contrast induced nephropathy and other outcomes (continued)

Author, year	Comparison	N	Population	Age, range of mean §	No. female (%)‡	Mean follow up	CM Route*	NAC route	Definition of CIN*	Study limitations †
Tepel, 2000 [75]	Placebo + 0.45% saline vs. NAC + 0.45% saline	83	CR concentration >1.2 mg per deciliter (or CrCl <50 ml per minute)	65-66	36 (43)	6 days	LOCM (Iopamidol) IV	Oral	A2	H
Thiele, 2010[76]	Placebo + NS vs. NAC + NS	251	Acute MI, STEMI	68	80 (32)	6 months	LOCM (Iopromide) IA	IV	A1	M
Webb, 2004[81]	Placebo + NS vs. NAC + NS	487	GFR <50 ml/min	70	190 (39)	3 days	LOCM (Ioversol) IA	IV	A1	L

%=percent; CIN=contrast-induced nephropathy; CKD=chronic kidney disease; CM=contrast media; CrCl=creatinine clearance; Cr=creatinine; eGFR=estimated glomerular filtration rate; GFR=glomerular filtration rate; HOCM=high osmolar contrast media; IA=intrarterial; ICU=intensive care unit; IOCM=iso-osmolar contrast media; IV=intravenous; LOCM=low-osmolar contrast media; mg/dl=milligram per deciliter; MI=myocardial infarction; ml/min=milliliter per minute; ml/min=milliliter per minute; mmol/l=millimole per liter; N=sample size; NAC=N-acetylcysteine; NR=not reported; NS=normal saline; PCI=percutaneous coronary intervention; STEMI=st elevation myocardial infarction; vs.=versus

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Percent females in entire study population
§ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table 5. Contrast induced nephropathy outcomes in studies comparing of N-acetylcysteine versus IV saline with or without placebo that are not included in the meta-analysis.

Author, year	Measure	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comp-rison* statistics at time point 1	Time Point 2	Time point 2 N ana-lyzed	n (%) with out-come at time-point 2	Comp-rison statist-cs at time point 2
ACT, 2011[1]	25% elevation of serum creatinine above baseline between 48 and 96 hours after angiography.	Placebo	1	48-96 hours	1119	142 (12.7)	1.00 (95% CI:0.81 to 1.25) p=.97				
ACT, 2011[1]	25% elevation of serum creatinine above baseline between 48 and 96 hours after angiography.	NAC	2		1153	147 (12.7)					
ACT, 2011[1]	Doubling in serum creatinine	Placebo	1	48-96 hours	1119	17 (1.5)	0.74 (95% CI:0.36 to 1.52)p=0.41				
ACT, 2011[1]	Doubling in serum creatinine	NAC	2		1153	13 (1.1)					
ACT, 2011[1]	Elevation >= 44.2 mol/L (0.5 mg/dL) in serum creatin	Placebo	1	48-96 hours	1119	42 (3.8)	RR: 1.04 (95% CI:0.69 to 1.57)p=.85				
ACT, 2011[1]	Elevation >= 44.2 mol/L (0.5 mg/dL) in serum creatin	NAC	2		1153	45 (3.9)					
ACT, 2011[1]	Elevation >=13.3 mol/L (0.3 mg/dL) in serum creatini	Placebo	1	48-96 hours	1119	123 (11)	RR: 1.10 (95% CI:0.88 to 1.39)p=.39				
ACT, 2011[1]	Elevation >=13.3 mol/L (0.3 mg/dL) in serum creatini	NAC	2		1153	140 (12.1)					
Awal, 2011[6]	Incidence of CIN	Normal Saline	1	24 hours	50	6 (12)	p=0.012				
Awal, 2011[6]	Incidence of CIN	NAC	2		50	0 (0)					

Evidence Table 5. Contrast induced nephropathy outcomes in studies comparing of N-acetylcysteine versus IV saline with or without placebo that are not included in the meta-analysis (continued).

Author, year	Measure	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comp-rison* statistics at time point 1	Time Point 2	Time point 2 N ana-lyzed	n (%) with out-come at time-point 2	Comp-rison statist-cs at time point 2
Baker, 2003[8]	Incidence of CIN	Normal Saline	1				OR, 0.27 (95% CI: 0.08 to 0.85), p=0.019	96 hours	39	8 (20.5)	Relative Risk: 0.28 (95% CI: 0.08 to 0.98), p=0.045
Baker, 2003[8]	Incidence of CIN	Saline + NAC	2						41	2 (4.9)	
Baranska-Kosakowska, 2007[84]		Hydration	1	NS	57	0					
Baraka-Kosakowska, 2007[84]		NAC	2		55	0					
Burns, 2010[16]	Incidence of CIN	Placebo	1	5 days	21	(14.3); P<0.05 vs nondiabetics within the same drug group (Fisher exact test)	p=0.61				
Burns, 2010[16]	Incidence of CIN	NAC	2		21	(4.8)					
Chouster man, 2011[20]	Incidence of CIN, AKIN serum creatinine definition only	Control	1	48 hours	70	15 (21)	Arm1 vs Arm2 Absolute difference: -13% (95% CI: -24, 1), p=0.033				
Chouster man, 2011[20]	Incidence of CIN, AKIN serum creatinine definition only	NAC	2		70	6 (9)					
Chouster man, 2011[20]	Incidence of CIN, classical CIN definition	Control	1	48 hours	70	15 (21)	Arm1 vs Arm2 Absolute difference: -7% (95% CI: -20, 6), p=0.27				
Chouster man, 2011[20]	Incidence of CIN, classical CIN definition	NAC	2		70	10 (14)					

Evidence Table 5. Contrast induced nephropathy outcomes in studies comparing of N-acetylcysteine versus IV saline with or without placebo that are not included in the meta-analysis (continued).

Author, year	Measure	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comp-rison* statistics at time point 1	Time Point 2	Time point 2 N ana-lyzed	n (%) with out-come at time-point 2	Comp-rison statist-cs at time point 2
Chousterman, 2011[20]	Incidence of CIN, whole AKIN definition	Control	1	48 hours	70	22 (31)	Arm1 vs Arm2 Absolute difference: 3% (95% CI: -21, 18), p=0.72				
Chousterman, 2011[20]	Incidence of CIN, whole AKIN definition	NAC	2		70	24 (34)					
Chousterman, 2013[21]	(AKIN definition) increase in serum creatinine of at least 0.3 mg/dLor increase to more than or equal to 50% from baseline and/or oliguria of less than 0.5 mL/kg per hour for more than 6 hours	Saline	1	48 hours	70	22 (31)	Absolute diff (95%), +3% (95% CI: -12 to 18), p=.72				

Evidence Table 5. Contrast induced nephropathy outcomes in studies comparing of N-acetylcysteine versus IV saline with or without placebo that are not included in the meta-analysis (continued).

Author, year	Measure	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comp-rison* statistics at time point 1	Time Point 2	Time point 2 N ana-lyzed	n (%) with out-come at time-point 2	Comp-rison statist-cs at time point 2
Chousterman, 2013[21]	(AKIN definition) increase in serum creatinine of at least 0.3 mg/dLor increase to more than or equal to 50% from baseline and/or oliguria of less than 0.5 mL/kg per hour for more than 6 hours	NAC	2		70	24 (34)					
Chousterman, 2013[21]	an increase in plasma creatinine of 0.3 mg/dl or more from baseline	Saline	1	48 hours	70	15 (21)	Absolute diff (95%), -7% (95% CI: -20 to 6), p=0.27				
Chousterman, 2013[21]	an increase in plasma creatinine of 0.3 mg/dl or more from baseline	Saline	1	48 hours	70	15 (21)	Absolute diff (95%), -13% (95% CI: -24 to -1), p=0.033				
Chousterman, 2013[21]	an increase in plasma creatinine of 0.3 mg/dl or more from baseline	NAC	2		70	10 (14)					
Chousterman, 2013[21] (continued)	an increase in plasma creatinine of 0.3 mg/dl or more from baseline	NAC	2		70	6 (9)					

Evidence Table 5. Contrast induced nephropathy outcomes in studies comparing of N-acetylcysteine versus IV saline with or without placebo that are not included in the meta-analysis (continued).

Author, year	Measure	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comp-rison* statistics at time point 1	Time Point 2	Time point 2 N ana-lyzed	n (%) with out-come at time-point 2	Comp-rison statist-cs at time point 2
Fung, 2004[26]	>25% SCr or >0.5 mg/dl	Hydration	1	during study period (within 48 hours post-procedure)		6 (13.3)	p=0.8				
Fung, 2004[26] (continued)	>25% SCr or >0.5 mg/dl	Hydration + NAC	2			8 (17.4)					
Kim, 2010[43]	an increase in serum creatinine concentration of at least 0.5 mg/dL or a greater than 25% within 48 h of contrast exposure	control	1	48 hours	86	7 (8.1)	p=NS				
Kim, 2010[43] (continued)	an increase in serum creatinine concentration of at least 0.5 mg/dL or a greater than 25% within 48 h of contrast exposure	NAC	2		80	3 (3.8)					

Evidence Table 5. Contrast induced nephropathy outcomes in studies comparing of N-acetylcysteine versus IV saline with or without placebo that are not included in the meta-analysis (continued).

Author, year	Measure	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comp-rison* statistics at time point 1	Time Point 2	Time point 2 N ana-lyzed	n (%) with out-come at time-point 2	Comp-rison statist-cs at time point 2
Koc, 2012[85]	baseline SCr ≥ 25% and/or an absolute increase in SCr of ≥ 0.5 mg/dL 48 hours after the procedure	Normal Saline	1	48 hours	60	6 (10)	All arms p=.012				
Koc, 2012[85]	baseline SCr ≥ 25% and/or an absolute increase in SCr of ≥ 0.5 mg/dL 48 hours after the procedure	NAC + high-dose saline	2		80	2 (2.5)					
Lawlor, 2007[86]	>25% SCr or >0.5 mg/dl	Placebo	1	48 hours	25	2 (8)	p=0.99				
Lawlor, 2007[86] (continued)	>25% SCr or >0.5 mg/dl	NAC+IV hydration	2		25	2 (8)					
Lawlor, 2007[86]	>25% SCr or >0.5 mg/dl	NAC+Oral hydration	3		28	2 (7)					
Sandhu, 2006[70]	>25% SCr or >0.5 mg/dl	Control	1	48 hours	53	0					
Sandhu, 2006[70]	>25% SCr or >0.5 mg/dl	NAC	2		53	3					
Webb, 2004[81]	> 44 umol/l in crease in serum creatinine, per protocol analysis	Placebo	1	2-8 days	204	(5.9)	p=0.69				
Webb, 2004[81]	> 44 umol/l in crease in serum creatinine, per protocol analysis	NAC	2		194	(7.2)					

Evidence Table 5. Contrast induced nephropathy outcomes in studies comparing of N-acetylcysteine versus IV saline with or without placebo that are not included in the meta-analysis (continued).

%=percent; A1=arm 1; A2=arm 2; A3=arm 3; AKIN=Acute Kidney Injury Network; CECT= contrast enhanced computed tomography; CI=confidence interval; CIN=contrast induced nephropathy; Cr=creatinine; GFR=glomerular filtration rate; H=hour; IA=intrarterial; IV=intravenous; Mg/dl=milligram per deciliter; N=sample size; NAC=N-acetylcysteine; NR=not reported; NS=non-signfiicant; OR=odds ratio; P=p-value; RR=relative risk; SCr=serum creatinine; SG=subgroups; Umol/l=micromole per liter

Evidence Table 6. Changes in serum creatinine outcomes in studies comparing of N-acetylcysteine versus placebo or usual care

Author year	Measure	SG	Interven-tions	Arm	Base-line N anal-yzed	Mean base-line value (SD)	Time point 1	Time point 1 N anal-yzed	Mean (SD)	Comp-arison* statistics at time point 1	Time point 2	Time point 2 N anal-yzed	Mean (SD)	Comp-arison statistics at time point 2	Time Point 3	Time point 3, N analyzed	Mean (SD)	Comp-arison statistics at time point 3
Buyukhatipoglu, 2010[87]	Change in serum creatinine, regression analysis	Contrast amount	Control	1			24 hours			Beta coefficient: 0.213, p=0.712 T-test: 0.371								
Buyukhatipoglu, 2010[87]	Change in serum creatinine, regression analysis	Contrast amount	NAC + saline	2														
Buyukhatipoglu, 2010[87]	Change in serum creatinine, regression analysis	NAC use	Control	1			24 hours			Beta-coefficient: 0.305, p=0.068 t-test: 1.877								
Buyukhatipoglu, 2010[87]	Change in serum creatinine, regression analysis	NAC use	NAC + saline	2														
Heng, 2008[88]	Change in serum creatinine, umol/l, from baseline		Placebo	1			2 days	32	-3 (28)	p=0.84								
Heng, 2008[88]	Change in serum creatinine, umol/l, from baseline		NAC	2				28	-2 (25)									

Evidence Table 6. Changes in serum creatinine outcomes in studies comparing of N-acetylcysteine versus placebo or usual care (continued)

Author year	Measure	SG	Interven-tions	Arm	Base-line N anal-yzed	Mean base-line value (SD)	Time point 1	Time point 1 N anal-yzed	Mean (SD)	Comp-arison* statistics at time point 1	Time point 2	Time point 2 N anal-yzed	Mean (SD)	Comp-arison statistics at time point 2	Time Point 3	Time point 3, N analyz ed	Mean (SD)	Comp-arison statistics at time point 3
Huber, 2006[89]	mg/dl			1	38	2.2 (.4)	12 hours				24 hours				48 hours			
Huber, 2006[89]	mg/dl		Theophylline	2	92	1.52 (0.43)	12 hours	51	1.19 (0.58)		24 hours	NR	NR		48 hours	1.16 (0.55)		
Huber, 2006[89]	mg/dl		Acetylcysteine	3	60	0.88 (0.2)		50	1.28 (0.75)			50				Median : 1.00		
Huber, 2006[89]	mg/dl		Theophylline + Acetylcysteine	4				NR				49				Median : <0.001		
Sar, 2010[90]	mg/dL		Saline	1	20	0.81 (0.17)	48 hours	20	0.94 (0.16)	p=0.03								
Sar, 2010[90]	mg/dL		Saline + NAC	2	25	0.83 (0.15)		25	0.79 (0.21)									
Staniloae, 2009[91]			no NAC	1	246	1.47 (0.36)	48-72 hours	246	1.57 (0.44)	p=0.12								
Staniloae, 2009[91]			NAC	2	168	1.43 (0.40)		168	1.51 (0.42)									
Wang, 2008[92]	Serum creatinine levels at baseline and follow-up		Saline	1	23	1.18 (0.50)	24 hours	23	1.09 (0.50)	p=0.27								
Wang, 2008[92]	Serum creatinine levels at baseline and follow-up		Saline + NAC	2	23	1.48 (0.81)		23	1.30 (0.74)									

CI=confidence interval; H=hours; Hrs=hours; IQR=interquartile range; IV=intravenous; LVEF=left ventricular ejection fraction; Mg/dl=milligram per deciliter; Mg=milligram; Ml=milliliter; N=sample size; NAC=N-acetylcysteine; NR=not reported; NS=non-significant; NS=non-significant; P=p-value; SCr=serum creatinine; SG=subgroups; Umol/l=micromole per liter; V=versus; Yrs=years;

Evidence Table 7. GFR levels in studies comparing of N-acetylcysteine versus placebo or usual care.

Author year	Measure	SG	Interven-tions	Arm	Base-line N analyzed	Mean base-line value (SD)	Time point 1	Time point 1 N analyzed	Mean (SD)	Comparison* statistics at time point 1	Time point 2	Time point 2 N analyzed	Mea n (SD)	Comparison statistics at time point 2
Sar, 2010[90]	mL/min		Saline	1	20	97.8 (28.6)	48 hours	20	99.4 (35.7)	p=0.021				
Sar, 2010[90]	mL/min		Saline + NAC	2	25	90.9 (25.1)		25	90.8 (25.0)					
Staniloae, 2009[91]	Mean change in eGFR		n NAC	1			45-120 hours	246	-3.32 (8.1)	p=0.51				
Staniloae, 2009[91]	Mean change in eGFR		NAC	2				168	-2.79 (7.8)					
Wang, 2008[92]	eGFR measured at baseline and after procedure		Saline	1	23	57.97 (26.38)	24 hours	23	63.00 (29.27)	p=0.71				
Wang, 2008[92]	eGFR measured at baseline and after procedure		Saline + NAC	2	23	59.54 (47.13)		23	68.10 (57.65)					

eGFR=estimated glomerular filtration rate; GFR=glomerular filtration rate; N=sample size; NAC=N-acetylcysteine; P=p-value; SD=standard deviation; SG=subgroups

Evidence Table 8. Summary of other outcomes reported in studies comparing N-acetylcysteine and placebo or usual care for the prevention of contrast-induced nephropathy

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
ACT, 2011[1]	Arm 1: Placebo+ NS Arm 2: NAC+ NS	At 30 days Arm1: 24/1135 (2.1) Arm2: 23/1171 (2.0) RR 0.97 (95% CI: 0.54-1.73); P=0.92	At 30 days Arm1: 3/1135 (0.3) Arm2: 3/1171 (0.3) RR 0.87 (95% CI: 0.17-4.35); P=0.86	NR	NR
Alioglu, 2013[2]	Arm 1: 0.45% saline Arm 2: NAC + 0.45% saline	NR	NR	NR	NR
Allaqaband, 2002[3]	Arm1: 0.45% saline Arm2: 0.45% saline + NAC Arm3: 0.45% saline + fenoldopam	NR	Time point: NR, 20 who developed CIN needed hemodialysis, no other details	NR	NR
Amini, 2009[4]	Arm 1: Placebo+ NS Arm 2: NAC+ NS	NR	NR	NR	NR
Aslanger, 2012[5]	Arm 1: Placebo+ NS Arm 2: high-dose NAC+ NS	NR	NR	NR	NR
Awal, 2011[6]	Arm 1: NS Arm 2: NAC+ NS	NR	NR	NR	NR
Azmus, 2005[7]	Arm 1: Placebo+ NS Arm 2: NAC+ NS	At 48 hours: 6/201 (3.0) Arm2: 5/196 (2.5); P=1.0	At 48 hours Arm1: 1/201 (0.5) Arm2: 1/196 (0.5); P=1.0	NR	NR
Baker, 2003[8]	Arm 1: NS Arm 2: NAC+ NS	NR	At 96 hours Arm1: 0/39 (0) Arm2: 0/41 (0); P=NR	NR	Pulmonary edema at 96 hours Arm1: 2/39 Arm2: 2/41; P=NR
Baskurt, 2009[9]	Arm1: NS Arm2: NS + NAC Arm3: NS + NAC + theophylline	NR	NR	NR	Major adverse cardiac events at 48 hours Arm1: 0/42 (0) Arm2: 0/73 (0) Arm3: 0/72 (0); P=NR
Boccalandro, 2003[11]	Arm 1: Placebo + 0.45% saline Arm 2: NAC + 0.45% saline	NR	NR	NR	NR
Briguori, 2002[14]	Arm 1: 0.45% saline Arm 2: NAC + 0.45% saline	NR	At 48 hours Arm1: 1/91 (1.1) Arm2: 0/92 (0); P=NR	NR	NR
Brueck, 2013[15]	Arm1: placebo + NS Arm2: IV-NAC+ NS Arm3: IA-NAC+ NS	NR	NR	NR	NR

Evidence Table 8. Summary of other outcomes reported in studies comparing N-acetylcysteine and placebo or usual care for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Burns, 2010[16]	Arm 1: Placebo+ NS Arm 2: NAC+ NS	At 5 days Arm1: 9/21 (42.9) Arm2: 6/21 (28.6); P=0.52	At 5 days Arm1: 0/21 (0) Arm2: 0/21 (0); P=NR	All patients (ICU) Arm1: 13.1 (7.9) Arm2: 24.4 (23.5); P=0.47 Survivors (ICU) Arm1: 13.7 (7.3) Arm2: 25.0 (24.9); P=0.65 All patients (hospital stay) Arm1: 41.5 (42.6) Arm2: 50.7 (23.6); P=0.71 Survivors (hospital stay) Arm1: 45.8 (27.8) Arm2: 57.2 (60.6); P=0.68	NR
Carbonell, 2007[17]	Arm 1: Placebo + 0.45% saline Arm 2: NAC + 0.45% saline	Time point: NR Arm1: 5/109 (4.6) Arm2: 3/107 (2.8); P=NR	NR	Coronary unit stay Arm1: median 4 (2-37) Arm2: median 4.5 (2-24); P=NR	NR
Carbonell, 2010[18]	Arm 1: Placebo + 0.45% saline Arm 2: NAC + 0.45% saline	Coronary unit Time point: short-term Arm1: 2/42 (4.2) Arm2: 3/39 (7.7) OR 0.20 (95% CI: 0.04-0.97) P=0.18 In-hospital Time point: short-term Arm1: 7/42 (16.7) Arm2: 4/39 (10.3); P=0.65 Long-term Arm1: 9/42 (21.4) Arm2: 6/39 (15.4); P=0.67	At 12 months Arm1: 1/42 (2.0) Arm2: 0/39 (0); P=0.15	Coronary unit stay Arm1: median 4 (2-27) Arm2: median 5 (1-20); P=0.70 Hospital Arm1: median 10 (2-76) Arm2: median 10 (1-42); P=0.20	NR
Castini, 2010[19]	Arm1: NS Arm2: NS + NAC Arm3: NaHCO3	NR	NR	NR	NR

Evidence Table 8. Summary of other outcomes reported in studies comparing N-acetylcysteine and placebo or usual care for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Chousterman, 2011[20]	Arm 1: NS Arm 2: NAC + NS	NR	NR	NR	NR
Chousterman, 2013[21]	Arm 1: NS Arm 2: NAC + NS	NR	Time point: NR Arm1: 5/54 (9) Arm2: 7/62 (11); P=NR	NR	NR
Demir, 2008[22]	Arm1:NS Arm2: NAC + NS Arm3: misopriatol + NS Arm4: theophylline + NS Arm5: nifedipine + NS	NR	NR	NR	NR
Durham, 2002[23]	Arm 1: 0.45% Saline Arm 2: high-dose NAC + 0.45% saline	NR	Whole population: 2/79 (2.4%) P=NR	NR	NR
Ferrario, 2009[24]	Arm 1: Placebo+ NS Arm 2: NAC+ NS	At 72 hours Arm1: 0/101 (0) Arm2: 0/99 (0); P=NR	At 72 hours Arm1: 0/101 (0) Arm2: 0/99 (0); P=NR	NR	NR
Fung, 2004[26]	Arm 1: NS Arm 2: NAC+ NS	NR	Temporary dialysis therapy for acute renal failure Time point: NR Arm1: 0/45 (0) Arm2: 0/46 (0); P=NR	NR	NR
Goldenberg, 2004[27]	Arm 1: Placebo + 0.45% Saline Arm 2: NAC + 0.45% saline	NR	NR	NR	Overt congestive heart failure following coronary angiography Time point: NR Arm1: 1/39 (3) Arm2: 1/41 (2); P=74
Gomes, 2005[28]	Arm 1: Placebo+ NS Arm 2: NAC+ NS	Time point: NR Arm1: 2/79 (2.5) Arm2: 5/77 (6.5); P=0.42	Time point: NR Arm1: 0/79 (0) Arm2: 2/77 (2.6); P=0.24	NR	NR
Gulel, 2005[30]	Arm 1: NS Arm 2: NAC+ NS	NR	NR	NR	NR
Gunebakmaz, 2012[31]	Arm1: NS Arm2: NS + nebivolol Arm3: NAC + NS	NR	NR	NR	NR
Holscher, 2008[34]	Arm1: NS + glucose Arm2: NS + dialysis + glucose Arm3: NS + NAC + glucose	NR	NR	NR	NR

Evidence Table 8. Summary of other outcomes reported in studies comparing N-acetylcysteine and placebo or usual care for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Hsu, 2007[35]	Arm 1: NS Arm 2: NAC+ NS	NR	Time point: NR Arm1: 0/9 (0) Arm2: 0/11 (0); P=NR	Arm1: 8.1 (4.1) Arm2: 5.2 (1.5); P=0.04	Acute coronary syndrome or acute congestive heart failure Time point: NR Arm1: 0/9 (0) Arm2: 0/11 (0); P=NR
Hsu, 2012[36]	Arm 1: NS Arm 2: NAC+ NS	Time point: NR Arm1: 13/103 (12.6) Arm2: 8/106 (7.5) OR 0.57 (95% CI: 0.224-1.427) P=NR	Time point: NR Arm1: 0/103 (0) Arm2: 0/106 (0); P=NR	NR	NR
Izani Wan Mohamed, 2008[37]	Arm 1: 0.45% Saline Arm 2: NAC + 0.45% saline	NR	Patients who developed CIN at 48 hours Arm1: 0/6 (0) Arm2: 0/2 (0); P=NR	NR	NR
Jaffery, 2012[38]	Arm 1: NS Arm 2: high-dose NAC+ NS	Time point: short-term Arm1: 1/192 (0.5) Arm2: 1/206 (0.5); P=1.0 At 30 days Arm1: 3/192 (1.6) Arm2: 3/206 (1.3); P=1.0	NR	Arm1: 3.6 (3.3) Arm2: 3.2 (2.6); P=0.13	NR
Kay, 2003[40]	Arm 1: Placebo + NS Arm 2: NAC+ NS	NR	NR	Arm1: 3.9 (2.0) Arm2: 3.4 (0.9) RR 0.52 (95% CI: 0.08-0.96) P=0.02	NR
Kefer, 2003[41]	Arm 1: Placebo + dextrose Arm 2: high-dose NAC + dextrose	NR	NR	NR	NR
Khalili, 2006[42]	Arm 1: NS Arm 2: NAC+ NS	NR	NR	NR	NR
Kim, 2010[43]	Arm 1: NS Arm 2: high-dose NAC+ NS	NR	NR	NR	NR
Kimmel, 2008[44]	Arm 1: Placebo + 0.45% Saline Arm 2: NAC + 0.45% saline	NR	NR	NR	NR

Evidence Table 8. Summary of other outcomes reported in studies comparing N-acetylcysteine and placebo or usual care for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Kinbara, 2010[45]	Arm1: NS Arm2: NS + aminophylline Arm3: NS + high-dose NAC	NR	NR	NR	NR
Kotlyar, 2005[47]	Arm1: NS Arm2: NAC 300mg + NS Arm3: NAC 600mg + NS	NR	Chronic reductions in renal function at 30 days Arm1: 2/19 (11) Arm2: 4/20 (20) Arm3: 2/21 (10); P=0.66	NR	NR
MacNeill, 2003[51]	Arm 1: Placebo + NS Arm 2: NAC+ NS	NR	NR	NR	NR
Marenzi, 2006[53]	Arm1: Placebo + NS Arm2: NAC + NS Arm3: High-dose NAC + NS	Time point: NR Arm1: 13/119 (11) Arm2: 5/115 (4) Arm3: 3/118 (3); P=0.007	Time point: NR Arm1: 6/119 (5) Arm2: 2/115 (2) Arm3: 1/118 (1); P=0.14	NR	NR
Miner, 2004[58]	Arm 1: Placebo + 0.45% Saline Arm 2: High-dose NAC + 0.45% saline	In-hospital Time point: NR Arm1: 2 Arm2: 0; P=NR Long-term Time point: NR Arm1: 3 (3.5) Arm2: 4 (4); P=NR	In-hospital Time point: NR Arm1: 0 Arm2: 1; P=NR Time point: NR Arm1: 1 Arm2: 1; P=NR	NR	Non-fatal MI, in-hospital Time point: NR Arm1: 1 Arm2: 6; P=0.14 Non-fatal MI, long-term Time point: NR Arm1: 4 Arm2: 6; P=NR
Ochoa, 2004 [60]	Arm 1: Placebo + NS Arm 2: NAC+ NS	NR	NR	NR	NR
Oldemeyer, 2003[61]	Arm 1: Placebo + 0.45% Saline Arm 2: High-dose NAC + 0.45% saline	NR	At 48 hours Arm1: 0/47 (0) Arm2: 0/48 (0); P=NR	Arm1: 4.9 (4.0) Arm2: 4.8 (3.8); P=NR	NR
Ozcan, 2007[62]	Arm1: NS Arm2: NS + NAC Arm3: bicarbonate	NR	At 48 hours Arm1: 1/88 (1.14) Arm2: 0/88 (0) Arm3: 1/88 (1.14); P=NR	NR	Incidence of congestive heart failure at 48 hours Arm1: 0/88 (0) Arm2: 0/88 (0) Arm3: 0/88 (0); P=NR
Poletti, 2007[65]	Arm 1: NS + 0.45% Saline Arm 2: High-dose NAC + 0.45% saline	NR	NR	NR	NR

Evidence Table 8. Summary of other outcomes reported in studies comparing N-acetylcysteine and placebo or usual care for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Ratcliffe, 2009[67]	Arm1: NS Arm2: NS + high-dose NAC Arm3: NaHCO3 Arm4: NaHCO3 + NAC	NR	NR	NR	NR
Reinecke, 2007 [68]	Arm1: NS + glucose Arm2: NS+ dialysis + glucose Arm3: NS+ NAC + glucose	In hospital Arm1: 1/NR (0.7) Arm2: 3/NR (2.2) Arm3: 1/NR (0.7); P=0.427 30-day Arm1: 3/NR (2.2) Arm2: 3/NR (2.2) Arm3: 1/NR (0.7); P=0.540 Months NR Arm1: 9.7 Arm2: 13.1 Arm3: 9.9; P=0.582	In-hospital Time point: NR Arm1: 1/NR (0.7) Arm2: 22/133 (1.5) Arm3: 1/NR (0.7); P=0.762	NR	NR
Sadat, 2011[69]	Arm1: NS Arm2: NS + NAC	NR	NR	NR	NR
Sandhu, 2006[70]	Arm 1: No treatment Arm 2: NAC	NR	NR	NR	NR
Seyon, 2007[71]	Arm 1: Placebo + 0.45% Saline Arm 2: NAC + 0.45% saline	NR	NR	NR	NR
Shyu, 2002[73]	Arm 1: 0.45% Saline Arm 2: NAC + 0.45% saline	NR	Time point: NR Arm1: 1 Arm2: 0; P=NR	NR	NR
Tanaka, 2011[74]	Arm 1: Placebo + Ringer's Lactate Arm 2: High-dose NAC + Ringer's Lactate	NR	NR	Arm1: 20.8 (8.9) Arm2: 18.7 (5.6); P=0.22	NR
Tepel, 2000 [75]	Arm 1: 0.45% Saline Arm 2: NAC + 0.45% saline	NR	NR	NR	NR

Evidence Table 8. Summary of other outcomes reported in studies comparing N-acetylcysteine and placebo or usual care for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Thiele, 2010[76]	Arm 1: Placebo + NS Arm 2: NAC+ NS	At 6 months Arm1: 12/125 Arm2: 12/126; P=NR	NR	NR	Non-fatal reinfarctions At 6 months Arm1: 4/125 (3.2) Arm2: 3/126 (2.4); P=NR New congestive heart failure at 6 months Arm1: 7 (5.6) Arm2: 11 (8.7); P=NR
Webb, 2004[81]	Arm 1: Placebo + NS Arm 2: NAC+ NS	At 8 days Arm1: 5/227 Arm2: 7/220; P=NR At >8 days Arm1: 4/227 Arm2: 3/220; P=NR	At 2-8 days Arm1: 0/227 Arm2: 0/220; P=NR	NR	NR

%=percent; ACT=Acetylcysteine for Contrast-Induced Nephropathy Trial; CI=confidence interval; CIN=contrast induced nephropathy; MI=myocardial infarction; N=sample size; NAC=N-acetylcysteine; NaHCO3=sodium bicarbonate; NR=not reported; OR=odds ratio; P=p-value; RR=risk ratio; RRT=renal replacement therapy

* n/N refers to number of events divided by number at risk.

Evidence Table 9. Adverse events in studies comparing of N-acetylcysteine versus placebo or usual care

Author, Year	Adverse events
Allaqaband,2002[3]	Other: Hypotension Fenoldopam reaction. Definition not reported
Azmus, 2005[7]	Other: Nausea: 3 cases placebo 7 cases NAC Vomitting: 1 case placebo 2 cases NAC Epigastric pain: 1 case placebo 1 case NAC
Baker,2003[8]	Other: Allergic reaction Itching, flushing or transitory rash in 14% of patients on NAC
Carbonell, 2007[17]	no patients presented AEs
Carbonell,2010[18]	No patients presented side effects
Castini, 2010[19]	only reported acute renal failure (necessitating HD, ultrafiltration or peritoneal dialysis never occurred.
Fung, 2004[26]	Anaphalaxis: No patient in the NAC group developed an allergic reaction or other adverse event that necessitated withdrawal of NAC. Other: , No patient in the NAC group developed an adverse event that necessitated withdrawal of NAC
Goldenberg, 2004[27]	Heart failure: 2 cases of Congestive heart failure-one in each group Anaphalaxis Other: Transient hypotension, 1 case in the acetylcysteine group,
Gulel, 2005[30]	Other: GI disturbances, 3 pts in control (12%) 4 pts in NAC group (16%) p>0.05,
Heng, 2008[88]	Heart failure: 1 in NAC group Anaphalaxis Other: diarrrhea, 1 in NAC group 2 in placebo group, dialysis, 0 in both groups, , some adverse events were also entered as outcomes
Hsu, 2007[35]	Other: Adverse events after NAC administration, None
Izani Wan Mohamed, 2008[37]	Other: mild gastrointestinal upset and nausea, 2 (4%) patients in Arm 2. Arm 1, one patient developed nausea only, ,
Jaffery, 2012[38]	Other: composite events in-hospital mortality, mechanical ventilation and acute renal failure requiring dialysis. 2 (1%) Control 3 (1.5%) NAC p=1 adverse event during IV NAC administration None data not separated for the composite events
Kimmel, 2008[44]	Other: Diarrhoea, Diarrhoea in Zinc group
MacNeill, , 2003[51]	Other: , "Acetylcysteine was well tolerated with no adverse events recorded."
Marenzi, 2006[53]	Other: Cardiopulmonary resuscitation, ventricular tachycardia, or ventricular fibrillation High-rate atrial fibrillation other High-degree conduction disturbances, Cardiogenic shock requiring intraaortic balloon counterpulsation,Acute pulmonary edema requiring mechanical ventilation listed under in-hospital complications

Evidence Table9. Adverse events in studies comparing of N-acetylcysteine versus placebo or usual care (continued)

Author, Year	Adverse events
Miner, 2004[58]	Other: profound thrombocytopenia, Profound thrombocytopenia platelet count 20,000 platelets/mL. NAC=2 Placebo=0 p=ns, blood transfusion, NAC=1 Placebo=2 p=NS other adverse events are our outcomes of intetrest
Ochoa, 2004[60]	Other: Procedurerelated hypotension requiring vasopressors and/or intraaortic balloon counterpulsation, 4 (11%) patients in Arm 2, and in 7 (16%) patients in Arm 1(P = 0.45, Nausea, 1 patient in Arm 1, Serious adverse effects, None
Oldemeyer, 2003[61]	Other: General symptoms, Placebo 0 NAC 8: GI symptoms 6 - headache 1- chest tightness 1,
Ozcan, 2007[62]	No AES related to tx
Rashid, 2004[93]	No patient present any AE due to NAC
Ratcliffe, 2009[67]	Other: Serious adverse events, No serious adverse events from any of the medications given or from the procedure itself,
Reinecke,2007[68]	adverse events reported as secondary outcome.
Tanaka, 2011[74]	Heart failure: Placebo 7/38NAC 4/38p NS Anaphalaxis: 1 pt in the NAC arm had vomitting
Tepel, 2000[75]	Other: GI discomfort-temporary 7% acetylcysteine 12% control group dizziness 10% acetylcysteine 7% control group dialysis 0
Webb, 2004[81]	reported on death and need for dialysis

%=percent; AE=adverse event; GI=gastro-intestinal; HD=hemodialysis; IV=intravenous; NAC=N-acetylcysteine; NR=not reported; NS=non-significant;

Evidence Table 10. Summary of studies comparing IV sodium bicarbonate versus IV saline for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N	Population included	Age, Range of means[§]	Sex, n female (%)[‡]	Mean followup	CM Route*	Definition of CIN*	Study limitations†
Boucek, 2013[12]	IV hypertonic saline vs. IV NaHCO3	120	Diabetes	63-67	30 (25)	2 days	LOCM IA or IV	A3	L
Brar, 2008[13]	IV normal saline vs. IV NaHCO3	323	Stable renal disease	65-76	128 (39)	6 months	LOCM (Ioxilan) IA	A2	L
Castini, 2010[19]	IV normal saline vs. IV NaHCO3 + dextrose	156	General	70-72	19 (5)	5 days	IOCM IA	A1	M
Gomes, 2012[29]	IV normal saline vs. IV NaHCO3 + dextrose	301	CR >1.2 mg/dl, GFR, <50 ml/min	64-64	83 (27)	48 hours	LOCM (Ioxaglate) IA	A2	H
Koc, 2013[46]	IV normal saline vs. IV NaHCO3	195	Diabetic	40-53	93 (47)	2 days	LOCM (Iohexol) IA	A3	M
Lee, 2011[48]	IV normal saline vs. IV NaHCO3	382	General	62-73	111 (29)	6 months	IOCM (Iodixanol) IA	A1	M
Masuda, 2007[55]	Normal saline vs. IV NaHCO3	59	Cr concentration >1.1mg/dl or estimated GFR <60 ml/min	75-76	23 (39)	2 days	LOCM (Iopamidol) IA	A3	M
Merten, 2004[57]	Normal saline + dextrose vs. IV NaHCO3 + dextrose	119	Stable renal insufficiency	66	16 (13)	2 days	LOCM (Iopamidol) Both IA and IV	A1	M
Motohiro, 2011[59]	IV normal saline vs. IV NaHCO3 + IV normal saline	155	GFR <60	71	47 (30)	1 month	LOCM (Iopamidol) IA	A3	M
Ozcan, 2007[62]	Normal saline vs. IV NaHCO3 + dextrose	264	General	40-87	67 (25)	2 days	LOCM (Ioxaglate) IA	A3	H
Ratcliffe, 2009 [67]	Normal saline + dextrose vs. IV NaHCO3 + dextrose	78	General	64-67	31 (39)	3 days	IOCM (Iodixanol) IA	A1	H
Ueda, 2011[78]	Normal saline vs. IV NaHCO3	59	Cr >1.1 mg/dl, eGFR <60ml/min	75-77	13 (22)	2 days	LOCM (Iohexol) IA	A3	H
Vasheghani, 2009[94]	IV normal saline vs. IV NaHCO3 + IV normal saline	265	General	62-63	45 (17)	5 days	IOCM (iodixanol), LOCM (Iohexol), HOCM (amidotrizoic acid) IA	A3	L
Vasheghani-Farahani, 2010[79]	0.45% saline vs. IV NaHCO3 + 0.45% saline	72	CHF	61	15 (20)	2 days	LOCM (Iohexol) IA	A3	L

Evidence Table 6a. Summary of studies comparing IV sodium bicarbonate versus IV saline for the prevention of contrast-induced nephropathy and other outcomes (continued)

%=percent; CHF=congestive heart failure; CIN=contrast induced nephropathy; CM=contrast media; Cr=creatinine; GFR=glomerular filtration rate; HOCM=high osmolar contrast media; IA=intrarterial; IOCM=iso-osmolar contrast media; IV=intravenous; LOCM=low osmolar contrast media; Mg/dl=milligram per deciliter; Ml/min=milliliter per minute; N=sample size; NaCl=sodium chloride; NaHCO3=sodium bicarbonate; NR=not reported; vs.=versus

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance; † Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias; ‡ Percent females in entire study population; § Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.; ;

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis.

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Briguori, 2007[95]	increase in serum creatinine >25% from baseline value after administration of contrast media		Saline plus NAC	2		111	11 (9.9)					
Briguori, 2007[95]	increase in serum creatinine >25% from baseline value after administration of contrast media		Bicarbonate plus NAC	3		108	2 (1.9)					
Briguori, 2007[95]	increase in serum creatinine >25% from baseline value after administration of contrast media		Saline plus ascorbic acid plus NAC	4		107	11 (10.3)					
Briguori, 2011[96]	Incidence of CIAKI		sodium bicarbonate + NAC	1	48 hours	146	30 (20.5)	0.47 (95% CI: 0.24 to 0.92)				
Briguori, 2011[96]	Incidence of CIAKI		RenalGuard: saline + NAC + RenalGuard System + furosemide	2		146	16 (11)					
Briguori, 2011[96]	Incidence of CIAKI	GFR<30 ml.min.1,73 m^2	sodium bicarbonate + NAC	1	48 hours	146	20 (29.5)	0.44 (95% CI: 0.19 to 0.98)				

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis (continued).

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Briguori, 2011[96]	Incidence of CIAKI	GFR<30 ml.min.1,73 m^2	RenalGuard: saline + NAC + RenalGuard System + furosemide	2		146	11 (15)					
Briguori, 2011[96]	Increase >0.5 mg/dl		sodium bicarbonate + NAC	1	48 hours	146	22	p=<0.001				
Briguori, 2011[96]	Increase >0.5 mg/dl		RenalGuard: saline + NAC + RenalGuard System + furosemide	2		146	9					
Briguori, 2011[96]	Increase >25%		sodium bicarbonate + NAC	1	48 hours	146	19 (13)	p=<0.001				
Briguori, 2011[96]	Increase >25%		RenalGuard: saline + NAC + RenalGuard System + furosemide	2		146	4 (2.7)					
Briguori, 2011[96]	Increase >50%		sodium bicarbonate + NAC	1	48 hours	146	11 (7.5)	p=<0.001				
Briguori, 2011[96] (continued)	Increase >50%		RenalGuard: saline + NAC + RenalGuard System + furosemide	2		146	1 (0.7)					
Briguori, 2011[96],	Incidence of CIAKI	CIAKI risk score >11	Bicarbonate plus NAC	1	48 hours	146	11(14)	OR, 0.45 (95% CI: 0.15 to 1.36)				

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis (continued).

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Briguori, 2011[96],	Incidence of CIAKI	CIAKI risk score >11	RenalGuard: saline + NAC + RenalGuard System + furosemide	2			146	5 (7)				
Cho, 2010[97]	Cr		Saline	1	72 hours	27	6	A1 v A2 p=0.78 A1 v A3 P=0.617 A1 v A4 P=0.342 A2 v A3 P=0.835 A2 v A4 P=0.525 A3 vA4 P=0.663				
Cho, 2010[97]	Cr		Bicarbonate plus saline	2		21	2					
Cho, 2010[97]	Cr		Oral fluids	3		22	1					
Cho, 2010[97]	Cr		Oral bicarbonates plus fluids	4		21	1					
Hafiz, 2012[98]	Incidence of CI-AKI		saline	2	48 hours	161	19 (11.8)	p=>0.05				
Hafiz, 2012[98]	Incidence of CI-AKI		bicarbonate	3		159	14 (8.8)					
Hafiz, 2012[98]	Incidence of CI-AKI	With NAC	saline	2	48 hours	81	8 (9.9)	P=>0				
Hafiz, 2012[98]	Incidence of CI-AKI	With NAC	bicarbonate	3		80	8 (10)					

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis (continued).

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Hafiz, 2012[98]	Incidence of CI-AKI	Without NAC	saline	2	48 hours	80	11 (13.8)	p=>0.05				
Hafiz, 2012[98]	Incidence of CI-AKI	Without NAC	bicarbonate	3		79	6 (7.6)					
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Age (increasing years)	Saline	2	48 hours			OR, 1.05 (95% CI: 1.02 to 1.08), p=0.001				
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Age (increasing years)	Bicarbonate	3								
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Anemia	Saline	2	48 hours			OR, 1.97 (95% CI: 0.42 to 9.29), p=0.390				
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Anemia	Bicarbonate	3								
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Contrast volume >3ml/kg	Saline	2	48 hours			OR, 1.10 (95% CI: 1.00 to 1.20), p=0.038				
Hafiz, 2012[98] (continued)	Risk factors associated with higher incidence of CI-AKI	Contrast volume >3ml/kg	Bicarbonate	3								
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Diabetes	Saline	2	48 hours			OR, 1.57 (95% CI: 0.69 to 3.55), p=0.281				
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Diabetes	Bicarbonate	3								

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis (continued).

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Diuretics	Saline	2	48 hours			OR, 3.4 (95% CI: 1.46 to 7.98), p=0.005				
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Diuretics	Bicarbonate	3								
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	female	Saline	2	48 hours			OR, 0.49 (95% CI: 0.21 to 1.13), p=0.095				
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	female	Bicarbonate	3								
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	GFR	Saline	2	48 hours			OR, 0.99 (95% CI: 0.98 to 1.01), p=0.435				
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	GFR	Bicarbonate	3								
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Higher baseline creatinine level	Saline	2	48 hours			OR, 0.64 (95% CI: 0.35 to 1.19), p=0.161				
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Higher baseline creatinine level	Bicarbonate	3								
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Use of ACE inhibi	Saline	2	48 hours			OR, 1.12 (95% CI: 0.51 to 2.50), p=0.775				

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis (continued).

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Hafiz, 2012[98]	Risk factors associated with higher incidence of CI-AKI	Use of ACE inhibi	Bicarbonate	3								
Klima, 2012[99]	Incidence of CIN	Creatinine increase >25%	saline	1	48	89	1 (1)	p=0.02				
Klima, 2012[99]	Incidence of CIN	Creatinine increase >25%	long term sodium bicarbonate	2		87	8 (9)					
Klima, 2012[99]	Incidence of CIN	Creatinine increase >25%	short term sodium bicarbonate	3		82	8 (10)					
Klima, 2012[99]	Incidence of CIN	Creatinine increase >44umol/l	saline	1	48 hours	89	1 (1)	p=0.03				
Klima, 2012[99]	Incidence of CIN	Creatinine increase >44umol/l	long term sodium bicarbonate	2		87	7 (8)					
Klima, 2012[99]	Incidence of CIN	Creatinine increase >44umol/l	short term sodium bicarbonate	3		82	6 (7)					
Maioli, 2008[100]	Absolute increase of at least 0.5mg/dl over baseline serum creatinine within 5 days after administration		Saline plus NAC	2	5 days	252	29 (11.5)	p=0.60				
Maioli, 2008[100]	Absolute increase of at least 0.5mg/dl over baseline serum creatinine within 5 days after administration		Bicarbonate plus oral NAC	3		250	25 (10)					

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis (continued).

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Maioli, 2011[101] (continued)	Incidence of CI-AKI	>75 years	Late hydration	2		36	15 (41.7)					
Maioli, 2011[101]	Incidence of CI-AKI	>75 years	Early hydration	3		38	8 (21.1)					
Maioli, 2011[101]	Incidence of CI-AKI	anterior myocardial infarction	No hydration	1	3 days	65	22 (33.8)	All arms p=0.07				
Maioli, 2011[101]	Incidence of CI-AKI	anterior myocardial infarction	Late hydration	2		63	16 (25.4)					
Maioli, 2011[101]	Incidence of CI-AKI	anterior myocardial infarction	Early hydration	3		61	12 (19.7)					
Maioli, 2011[101]	Incidence of CI-AKI	Diabetes mellitus	No hydration	1	3 days	34	10 (29.4)	p=0.24 all arms				
Maioli, 2011[101]	Incidence of CI-AKI	Diabetes mellitus	Late hydration	2		31	11 (35.5)					
Maioli, 2011[101]	Incidence of CI-AKI	Diabetes mellitus	Early hydration	3		31	5 (16.1)					
Maioli, 2011[101]	Incidence of CI-AKI	eGFR <60ml/min	No hydration	1	3 days	34	10 (29.4)	All arms p=0.14				
Maioli, 2011[101]	Incidence of CI-AKI	eGFR <60ml/min	Late hydration	2		46	12 (26.1)					
Maioli, 2011[101]	Incidence of CI-AKI	eGFR <60ml/min	Early hydration	3		40	6 (15.0)					
Maioli, 2011[101]	Incidence of CI-AKI	High CIN risk	No hydration	1	3 days	52	18 (34.6)	All arms p=0.28				
Maioli, 2011[101]	Incidence of CI-AKI	High CIN risk	Late hydration	2		46	14 (26.1)					
Maioli, 2011[101] (continued)	Incidence of CI-AKI	High CIN risk	Early hydration	3		45	11 (24.4)					
Maioli, 2011[101]	Incidence of CI-AKI	Left ventricular ejection fraction <40%	No hydration	1	3 days	61	24 (39.3)	All arms p=0.04				

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis (continued).

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Maioli, 2011[101]	Incidence of CI-AKI	Left ventricular ejection fraction <40%	Late hydration	2		58	20 (34.5)					
Maioli, 2011[101]	Incidence of CI-AKI	Left ventricular ejection fraction <40%	Early hydration	3		56	12 (21.4)					
Maioli, 2011[101]	Incidence of CI-AKI	Volume of contrast media to eGFR ratio >3.7%	No hydration	1	3 days	50	15 (30.0)	All arms p=0.20				
Maioli, 2011[101]	Incidence of CI-AKI	Volume of contrast media to eGFR ratio >3.7%	Late hydration	2		55	15 (27.3)					
Maioli, 2011[101] (continued)	Incidence of CI-AKI	Volume of contrast media to eGFR ratio >3.7%	Early hydration	3		48	9 (18.8)					
Maioli, 2011[101]	Incidence of CI-AKI, whole population		No hydration	1	3 days	150	41 (27.3)	p=0.001 all arms				
Maioli, 2011[101]	Incidence of CI-AKI, whole population		Late hydration	2		150	34 (22.7)					
Maioli, 2011[101]	Incidence of CI-AKI, whole population		Early hydration	3		150	18 (12.0)					
Pakfetrat, 2009[102]	Development of CIN associated kidney injury using rifles criteria		Saline	1	48 hours	96	16 (16.6)	All arms p=0.4				
Pakfetrat, 2009[102]	Development of CIN associated kidney injury using rifles criteria		Bicarbonate plus saline	2		96	4 (4.2)					
Pakfetrat, 2009[102]	Development of CIN associated kidney injury using rifles criteria		Saline plus acetazolamide	3		94	5 (5.3)					

Evidence Table 11. Contrast-induced nephropathy outcomes in studies comparing of IV sodium bicarbonate and IV saline placebo that are not included in the meta-analysis (continued).

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Schmidt, 2007[103]	impairment of renal function occurring within 72 hours of administering contrast media, indicated by an absolute increase in the serum creatinine level of 0.5 mg/dL or more.		NAc plus bicarbonate	2	72 hours	47	7 (14.9)	p=0.71				
Schmidt, 2007[103]	impairment of renal function occurring within 72 hours of administering contrast media, indicated by an absolute increase in the serum creatinine level of 0.5 mg/dL or more.		NAC plus saline	3		49	6 (12.2)					
Tamura, 2009[104]	increase >25% or >0.5 mg/dl in serum Cr within the first 3 days after the procedure compared to baseline value		saline	1	3 days	72	9 (12.5)	p=0.17				
Tamura, 2009[104]	increase >25% or >0.5 mg/dl in serum Cr within the first 3 days		Saline+bicarbonate	2		72	1 (1.4)					

	after the procedure compared to baseline value											
Vasheghani-Farahani, 2009[94]	absolute (0.5 mg/dL) or relative (25%) increase over baseline creatinine level 48 hours after expo-sure to a contrast agent.		saline	1	2 days	130	7 (5.9)	OR ?? (95% CI: 0.45 to 3.5) p=0.6	5 days	130	8 (6.6)	OR ?? (95% CI: 0.4-4.2) p=0.60
Vasheghani-Farahani, 2009[94]	absolute (0.5 mg/dL) or relative (25%) increase over baseline creatinine level 48 hours after expo-sure to a contrast agent.		Saline+bicarbonate	2		135	9 (7.4)			135	11 (8.5)	
Vasheghani-Farahani, 2009[94]	at least a 25% decrease in baseline eGFR 48 hours after contrast exposure		saline	1	2 days	130	3 (2.6)	OR 1.26(95% CI: 0.6 to 9.3) p=0.3	5 days	130	5 (4.2)	OR1.30(95% CI: 0.4 to 4.2) p=0.60
Vasheghani-Farahani, 2009[94]	at least a 25% decrease in baseline eGFR 48 hours after contrast exposure		Bicarbonate plus saline	2		135	7 (5.9)			135	7 (5.5)	

%=percent; A1=arm 1; A2=arm 2; A3=arm 3; A4=arm 4; ACE inhibi= angiotensin converting enzyme inhibitor; CI=confidence interval; CIAKI=contrast induced acute kidney injury; CIN=contrast induced nephropathy; CKD=chronic kidney disease; Cr=creatinine; CrCl=creatinine clearance; eGFR=estimated glomerular filtration rate; GFR=glomerular filtration rate; H=hour; HD=hemodialysis; Kg=kilogram; LVEF=left ventricular ejection fraction; Mg/dl=milligram per deciliter; ml/min/1.73m^2=milliliter per minute per 1.73m squared; ml=milliliter; Mmol/l=millimole per liter; N=sample size; NAC=N-acetylcysteine; NS=non-significant; OR=odds ratio; P=p-value; RR=relative risk; SCr=serum creatinine ; SG=subgroup; Umol/l=micromole per liter;

Evidence Table 12. Changes in serum creatinine outcomes in studies comparing of IV sodium bicarbonate and IV saline.

Author year	Measure	SG	Intervention	Arm	Baseline N analyzed	Mean baseline value (SD)	Time point 1	Time point 1 N analyzed	Mean (SD)	Comparison* statistics at time point 1
Adolph, 2008[105]	Short term		Saline plus dextrose	1	74	Mean (.35) (Max: 2.60 Min: 1.20)	2 days	74	Mean (.40) (Max: 3.14 Min: 1.05)	p=NS
Adolph, 2008[105]	Short term		Bicarbonate plus dextrose	2	71	Mean (0.51) (Max: 4.60 Min: 1.20)		71	Mean (.52) (Max: 4.86 Min: 0.99)	

%=percent; CrCl=creatinine clearance; eGFR=estimated glomerular filtration rate; H=hour; IQR=interquartile range; LVEF=left ventricular ejection fraction; Max=maximum; Mg/dl=milligram per deciliter; Min=minimum; Ml/min=milliliter perminute; N=sample size; NAC=N-acetylcysteine; NaCl=sodium chloride; NR=not reported; NS=non-significant; P=p-value; SD=standard deviation; SG=subgroups; SrCr=serum creatinine; Umol/l=micromole per liter; V=versus;

Evidence Table 13. Summary of other outcomes reported in studies comparing IV sodium bicarbonate and IV saline for the prevention of contrast-induced nephropathy

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Boucek, 2013[12]	Arm 1: 5.85 % Normal saline Arm 2: NaHCO3	At 1 month Arm1: 0/59 (0) Arm2: 0/61 (0) P=NR	Post-procedure within 1 month Arm1: 0/59 (0) Arm2: 0/61 (0) P=NR After 1 month Arm1: 2/59 (3.39) Arm2: 1/61 (1.64) P=NR	Duration of hospitalization Arm1: 8.4 (12.9) Arm2: 8.0 (10.0) P=NR	NR
Brar, 2008[13]	Arm1: IV normal saline Arm 2: NaHCO3	At 6 months Arm1: 7/165 (3.9) Arm2: 4/158 (2.3) P=0.54	At 1 month Arm1: 2/165(2) Arm2: 1/158 (1) P=NR At 6 months Arm1: 4/165 (2) Arm2: 2/158 (1) P=NR	NR	NR
Castini, 2010[19]	Arm1: IV normal saline Arm 2: NaHCO3 + dextrose	NR	NR	NR	NR
Gomes, 2012[29]	Arm1: IV normal saline Arm 2: NaHCO3 + dextrose	In-hospital mortality, short-term at 48 hours Arm1: 5/151 (3.4) Arm2: 7/150 (4.7) P=0.81	At 48 hours Arm1: 0/151 (0) Arm2: 0/150 (0) P=NR	Arm1: 8.6 (9.7) Arm2: 7.5 (10) P=0.35	NR
Koc, 2013[46]	Arm1: IV normal saline Arm 2: NaHCO3	NR	NR	NR	NR

Evidence Table 13. Summary of other outcomes reported in studies comparing IV sodium bicarbonate and IV saline for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Lee, 2011[48]	Arm1: IV normal saline Arm 2: NaHCO3	All-cause at 1 month Arm1: 0/189 (0) Arm2: 1/193 (0.5) P=1.0 At 1-6 months Arm1: 2/189 (1.1) Arm2: 5/193 (2.6) P=0.45 Cumulative at 6 months Arm1: 2/189 (1.1) Arm2: 6/193 (3.1) P=0.45	At 1 month Arm1: 1/189 (0.5) Arm2: 1/193 (0.5) P=1.0 At 1-6 month Arm1: 0/189(0) Arm2: 3/193 (1.6) P=0.25 At 6 months Arm1: 1/189 (0.5) Arm2: 4/193 (2.1) P=0.37	NR	Myocardial infarction at 1 month Arm1: 0/189 (0) Arm2: 0/1193 (0) P=NR At 1-6 month Arm1: 0/189 (0) Arm2: 0/1193 (0) P=NR At 6 months Arm1: 0/189 (0) Arm2: 0/193 (0) P=NR
Masuda, 2007[55]	Arm 1: Normal saline Arm 2: IV NaHCO3	At 48 hours Arm1: 2/29 (7) Arm2: 0/30 (0) P=0.24	Time point: NR Arm1: 3/29 (10) Arm2: 1/30 (3) P=0.35	NR	NR
Merten, 2004[57]	Arm 1: Normal saline + dextrose Arm 2: IV NaHCO3 + dextrose	NR	NR	NR	NR
Motohiro, 2011[59]	Arm 1: IV normal saline Arm 2: IV NaHCO3 + IV normal saline	NR	Time point: NR Arm1: 0/77 (0) Arm2: 0/78 (0) P=NR	NR	NR
Ozcan, 2007[62]	Arm 1: Normal saline Arm 2: Normal saline + NAC Arm 2: IV NaHCO3 + dextrose	NR	At 48 hours Arm1: 1/88 (1) Arm2: 0/88 (0) Arm3: 1/88 (1) P=NR	NR	Congestive heart failure at 48 hours Arm1: 0/88 Arm2: 0/88 Arm3: 0/88 P=NR
Ratcliffe, 2009 [67]	Arm 1: Normal saline + dextrose Arm 2: IV NaHCO3 + dextrose	NR	NR	NR	NR
Ueda, 2011[78]	Arm 1: Normal saline Arm 2: IV NaHCO3	Time point: NR Arm1: 3/29(10) Arm2: 2/30 P=NR	NR	Time point: NR Arm1: 22.8 (17.9) Arm2: 21.4 (19.6) P=0.78	NR
Vasheghani, 2009[94]	Arm 1: IV normal saline Arm 2: IV NaHCO3 + IV normal saline	NR	NR	NR	NR
Vasheghani-Farahani, 2010[79]	Arm 1: 0.45% saline Arm 2: IV NaHCO3 + 0.45% saline	NR	NR	NR	NR

Evidence Table 13. Summary of other outcomes reported in studies comparing IV sodium bicarbonate and IV saline for the prevention of contrast-induced nephropathy (continued)

%=percent; N=sample; NaCl=sodium chloride; NaHCO3=sodium bicarbonate; NR=not reported; NS=normal saline; P=p-value; RRT=renal replacement therapy; SD=standard deviation;

Evidence Table 14 – Adverse events in studies comparing IV sodium bicarbonate versus IV saline

Author, Year	Adverse events
Boucek, 2013[12]	Other: local bleeding at the site of arterial puncture, Local bleeding at the site of arterial puncture necessitating transfusion and/or surgical intervention. No significant difference in occurrence between the two groups.
Brar, 2008[13]	Myocardial infarction: 2 cases within 6 months in sodium bicarbonate group and 4 cases in sodium chloride group CVA: 1 case within 6 months in sodium bicarbonate group and 7 cases in sodium chloride group
Castini, 2010[19]	only reported acute renal failure (necessitating HD, ultrafiltration or peritoneal dialysis never occurred.
Cho, 2010[97]	Other: in-house mortality 0 in all arms
Masuda, 2007[55]	Heart failure: 22 cases of heart failure within 2 days of admission, 11 in each group Anaphalaxis acute renal failure requiring hemodialysis: 4 cases in total 1 in sodium bicarbonate group and 3 in sodium chloride group Circulatory failure with lactic acidosis: 10 cases in total 4 in sodium bicarbonate group and 6 in sodium chloride group Respiratory failure requiring mechanical ventilation: 8 cases in total 3 in sodium bicarbonate group and 5 in sodium chloride group
Ozcan, 2007[62]	No AES related to tx
Ratcliffe, 2009[67]	Other: Serious adverse events, No serious adverse events from any of the medications given or from the procedure itself
Ueda, 2011[78]	Heart failure: 5 patients in NaBicarbonate6 Patients in Na Chloride Anaphalaxis

AE=adverse events; CVA=cardiovascular accident; HD=hemodialysis; Na=sodium; NR=not reported

Evidence Table 15. Summary of studies comparing N-acetylcysteine plus IV normal saline versus IV sodium bicarbonate for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N randomized (N analyzed)	Population	Age (years) or range of means §	Number. female (%)‡	Total followup	CM route	Primary definition of CIN*	Study limitations†
Castini, 2010[19]	IV normal saline Oral NAC +IV normal saline IV NaHCO3 in 5% dextrose in water without NAC	156 (156)	Baseline SrCr 1.2 to 4 mg/dl.	70-73	19 (12)	5 days (labs were drawn at 24 hours, 48 hours, and at 5 days after the procedure)	IOCM (Iodixanol) IA	A1 (secondary endpoint: A2)	M
Heguilen, 2013[33]	IV NaHCO3 in 5% dextrose in water NAC + normal saline in 5% dextrose in water without NAC	133 (123)	Stable SrCr 1.25 mg/dl (110 micromol/l) to 4.5 mg/dl (364.5 micromol/l), or Cockcroft-Gault-estimated creatinine clearance 45 ml/min	65-69	34 (28)	2-3 days	LOCM (Ioversol) IA	A1	M
Ozcan, 2007[62]	Oral NAC + IV normal saline IV NaHCO3 in 5% dextrose in water without NAC	264 (NR)	Baseline SrCr >1.2 to 4 mg/dl	67-70	67 (25)	48 hours	LOCM (Ioxaglate) IA	A3	H
Ratcliffe, 2009 [67]	IV and oral NAC + IV normal saline in 5% dextrose IV NaHCO3 in 5% dextrose without NAC	118 (78)	Renal insufficiency and/or diabetes mellitus (renal insufficiency defined asSrCr > 132.6 µmol/L	66	31 (40)	7 days (labs were drawn at 24, 72, and 168 hours after the procedure)	IOCM (Iodixanol) IA	A1*	H

			(1.5 mg/dl) in men, and > 114.9 µmol/L(1.3 mg/dl) in women) or reduced calculated creatinine clearance (< 1.002 mL/s) using Cockcroft-Gault formula)						
Shavit, 2009[72] (prospective, partially blinded trial)	IV NaHCO3 in 5% dextrose in water oral NAC + intravenous normal saline	93 (87)	CKD stage III–IV (estimated glomerular filtration rate 15-60 mL/min calculated by the MDRD formula)	71-72	19 (22)	48 hours	LOCM (Iopamidol) IA	A1 (authors also used a definition of SrCr increase of > 0.3 mg/dL)	H

Evidence Table 16. Contrast-induced nephropathy outcomes in the study comparing N-acetylcysteine plus IV saline versus IV sodium bicarbonate that was not included in the meta-analysis.

Author, year	CIN definition	Intervention	Arm	Time point 1	Time point 1 N analyzed	N (%) with outcome at time point 1	Comparison statistics at time point 1
Shavit, 2009[72]	Increase in SrCr ≥ 25% from baseline	IV NaHCO3 in 5% dextrose in water	1	48 hours	51	5 (9.8)	p=NS
Shavit, 2009[72]	Increase in SrCr ≥ 25% from baseline	Oral NAC + intravenous normal saline	2		36	3 (8.3)	
Shavit, 2009[72]	Increase in plasma creatinine of ≥ 0.3 mg/dL or more from baseline	IV NaHCO3 in 5% dextrose in water	1	48 hours	51	8 (15.7)	p=NS
Shavit, 2009[72]	Increase in plasma creatinine of ≥ 0.3 mg/dL or more from baseline	Oral NAC + intravenous normal saline	2		36	6 (16.7)	

%=percent; A1=arm 1; A2=arm 2; A3=arm 3; CI=confidence interval; CIN=contrast-induced nephropathy; SrCr=creatinine; GFR=glomerular filtration rate; H=hour; Mg/dl=milligram per deciliter; N=sample size; NAC=N-acetylcysteine; NaCl=sodium chloride; NaHCO3=sodium bicarbonate; NS=non-significant; RR=risk ratio; SrCr=serum creatinine

Evidence Table 17. Summary of other outcomes reported in studies comparing N-acetylcysteine plus IV saline versus IV sodium bicarbonate for the prevention of contrast-induced nephropathy

Author, year	Comparison	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Castini, 2010[19]	Arm1: IV normal saline Arm2: Oral NAC + IV normal saline Arm3: IV NaHCO3 in 5% dextrose in water	0/156 (0)	-0/156 (0)	NR	NR
Heguilen, 2013[33]	Arm 2: IV NaHCO3 in 5% dextrose in water Arm 3: NAC + IV NaHCO3 in 5% dextrose in water Arm 4: NAC + IV normal saline in 5% dextrose in water	NR	NR	NR	Heart failure at 48 hours: Arm 1: 0/80 (0) Arm 2: 0/43 (0) Arm 3: 0/38 (0)
Ozcan, 2007[62]	Arm1: IV normal saline Arm2: Oral NAC + IV normal saline Arm3: IV NaHCO3 in 5% dextrose in water	NR	At 48 hours Arm1: 1/88 (1) Arm2: 0/88 (0) Arm3: 1/88 (1); p=NR	NR	Congestive heart failure at 48 hours 0/264 (0)
Ratcliffe, 2009 [67]	Arm1: IV normal saline in 5%dextrose in water Arm2: IV and oral NAC + IV normal saline in 5% dextrose in water Arm3: IV NaHCO3 in 5% dextrose in water Arm4: IV and oral NAC + IV NaHCO3 in 5% dextrose in water	NR	NR	NR	NR
Shavit, 2009 [72]	Arm1: IV NaHCO3 in 5% dextrose in water Arm2: Oral NAC + intravenous normal saline	NR	0/87 (0)	NR	NR

%=percent; CIN=contrast-induced nephropathy; CKD=chronic kidney disease; CM=contrast media; H=high risk; IA=intrarterial; IV=intravenous; M=moderate risk; Mg/dl=milligram per deciliter; MDRD=Modification of Diet in Renal Disease; N=sample size; NAC=N-acetylcysteine; NaHCO3=sodium bicarbonate; SrCr=serum creatinine;

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1);> 25% (A1*); ≥0.5 mg/dl (A2); ->25% or 0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Percent females in entire study population
§ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms if the mean age for the whole population is not reported.

*n/N refers to number of events divided by number at risk.

Evidence Table 18. Reported adverse events in studies comparing N-acetylcysteine plus IV saline versus IV sodium bicarbonate

Author, Year	Adverse events
Castini, 2010[19]	Acute renal failure necessitating HD, ultrafiltration or peritoneal dialysis did not occur.
Heguilen,2013[33]	Volume administration resulted in a moderate although not significantly different increase among the three groups in both systolic and diastolic blood pressure, but none of the patients who completed the study developed heart failure or respiratory distress (ten patients did not complete the study; seven of those were lost to follow-up).
Ozcan, 2007[62]	No adverse events were reported to have occurred related to active treatments.
Ratcliffe, 2009[67]	There were no reported serious adverse events from any of the medications given or from the procedure itself.
Shavit, 2009[72]	No patient developed more than a 50% rise in serum creatinine or required renal replacement therapy during the hospitalization.

HD=hemodialysis

Evidence Table 19. Summary of studies comparing statins plus IV fluids versus IV fluids with or without placebo for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N	Population included	No. female (%)‡	Age, range of means§	Mean followup	CM Route*	Definition of CIN*	Study limitations†
Han, 2013[32]	IV normal saline vs. rosuvastatin +IV NS (hydration at discretion of clinicians)	2998	T2DM and stage 2-3 CKD	1044 (34)	61	72 hours CIN 30 days other	IOCM Iodixanol IA	A3	H
Jo, 2008[39]	Placebo + IV 0.45% saline vs. Simvastatin + IV 0.45% saline	247	≥Stage 3 CKD (CrCl≤ 60 ml/min or SrCr ≥1.1 mg/dl)	68 (38)	65-66	48 hr (Sr Cr/CIN) 1 and 6 months, other outcomes	IOCM Iodixanol IA	A3	M
Li, 2012 [50]	Placebo (undefined) + IV normal saline vs. atorvastatin + IV normal saline	161	ACS: acute STEMI	39 (24)	65-66	72 hr (CIN) 1 month (other outcomes)	LOCM Iopromide IA	A3	M
Ozhan, 2010[63]	NAC + IV normal salinevs. NAC + Atorvastatin +IV normal saline	130	General	53 (40)	54-55	48 hours	LOCM Iopamidol IA	A3	M
Patti, 2011[64]	Placebo vs. Atorvastatin (All patients received aspirin (100 mg/day) and clopidogrel 600-mg load >3 hours before the procedure)	241	ACS: unstable angina, or non-STEMI (statin naïve)	54 (22)	65-66	48 hours	LOCM Iobitridol IA	A3	L
Quintavalle, 2012[66]	NAC + IV $NaHCO_3$ vs. atorvastatin + NAC + IV $NaHCO_3$	410	≥Stage 3 CKD	187 (45)	70	48 hrs (CIN) 1 year (other outcomes)	IOCM Iodixanol IA	A1	M
Toso, 2010[77]	Placebo + IV normal saline + NAC vs. atorvastatin + IV normal saline + NAC	304	≥Stage 3 CKD	108 (35)	75-76	Within 5 days (CIN) 1 month (other outcomes)	IOCM Iodixanol IA	A2	M
Xinwei, 2009[82]	Simvastatin 20mg + IV normal saline vs.simvastatin 80mg + IV normal saline	228	ACS: unstable angina, STEMI, or non-STEMI	146 (64)	65-66	48 hours	IOCM Iodixanol IA (patients with CKD) LOCM Iohexol IA (other patients)	A3	M

Evidence Table 19. Summary of studies comparing statins plus IV fluids versus IV fluids with or without placebo for the prevention of contrast-induced nephropathy and other outcomes

%=percent; ACS=acute coronary syndrome; CIN=contrast induced nephropathy; CKD=chronic kidney disease; CM=contrast media; IA=intrarterial; IOCM=iso-osmolar contrast media; LOCM=low osmolar contrast media; Mg/dl=milligram per deciliter; N=sample size; NAC=N-acetylcysteine; NaHCO3=sodium bicarbonate; NR=not reported; NS=normal saline; STEMI=ST Elevation Myocardial Infarction; T2DM=type 2 diabetes mellitus; vs.=versus

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Percent females in entire study population
§ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table 20. Contrast induced nephropathy outcomes in studies comparing statin plus IV saline versus IV saline with or without placebo that are not included in the meta-analysis

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Ozhan, 2010[63]	Incidence of CIN		NAC + IV normal saline	2	48 hours	70	7 (10)	p=0.135				
Ozhan, 2010[63]	Incidence of CIN		NAC + Atorvastatin +IV normal saline	3		60	2 (3.3)					
Quintavalle, 2012[66]	Increase in serum creatinine >0.5mg.dl		NAC + IV NaHCO3	2	48 hours	208	16 (7.7)	p=0.085				
Quintavalle, 2012[66]	Increase in serum creatinine >0.5mg.dl		Atorvastatin + NAC + IV NaCO3	3		202	7 (3.5)					
Quintavalle, 2012[66]	Increase in serum creatinine >25% from baseline		NAC + IV NaHCO3	2	48 hours	208	14 (7)	p=0.10				
Quintavalle, 2012[66]	Increase in serum creatinine >25% from baseline		Atorvastatin + NAC + IV NaCO3	3		202	6 (3)					
Toso, 2010[77]	Incidence of CIN, primary definition		Placebo + IV normal saline + NAC	1	5 days		16 (11)	p=0.86				
Toso, 2010[77]	Incidence of CIN, primary definition		atorvastatin + IV normal saline + NAC	2			15 (10)					
Toso, 2010[77]	Incidence of CIN, secondary definition		Placebo + IV normal saline + NAC	1	5 days	152	(15)	p=0.67				
Toso, 2010[77]	Incidence of CIN, secondary definition		atorvastatin + IV normal saline + NAC	2		152	(17)					

Evidence Table 20. Contrast induced nephropathy outcomes in studies comparing statin plus IV saline versus IV saline with or without placebo that are not included in the meta-analysis

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Toso, 2010[77]	incidence of CIN	Age >=75 years	Placebo + IV normal saline + NAC	1	5 days	97	12 (12)	p=0.98				
Toso, 2010[77]	incidence of CIN	Age >=75 years	atorvastatin + IV normal saline + NAC	2		80	10(13)					
Toso, 2010[77]	Incidence of CIN	High-very High CIN risk score (>=11)	Placebo + IV normal saline + NAC	1	5 days	65	4 (6)	p=0.63				
Toso, 2010[77]	Incidence of CIN	High-very High CIN risk score (>=11)	atorvastatin + IV normal saline + NAC	2		57	6 (11)					
Toso, 2010[77]	Incidence of CIN	LVEF <40%	Placebo + IV normal saline + NAC	1	5 days	49	10 (20)	p=0.37				
Toso, 2010[77]	Incidence of CIN	LVEF <40%	atorvastatin + IV normal saline + NAC	2		41	4 (10)					
Xinwei, 2009[82]	postprocedure increase in serum creatinine of >/= 44.2 umol/L (0.5 mg/dl) or >25% from baseline	Simvastatin 20mg + IV NS	2	24 hours	115	16 (13.9)	p<0.5	48 hours	115	18 (15.7)	p<0.5	
Xinwei, 2009[82]	postprocedure increase in serum creatinine of >/= 44.2 umol/L (0.5 mg/dl) or >25% from baseline	Simvastatin 80mg + IV NS	3	24 hours	113	6 (5.3)			113	6 (5.3)		

Evidence Table 20. Contrast induced nephropathy outcomes in studies comparing statin plus IV saline versus IV saline with or without placebo that are not included in the meta-analysis

%=percent; CI=confidence interval; CIN=contrast induced nephropathy; CRF=chronic renal failure; GFR=glomerular filtration rate; Hrs=hours; LVEF=left ventricular ejection fraction; Mg/dl=milligram per deciliter; Mg=milligram; N=sample size; OR=odds ratio; P=p-value; SCr=serum creatinine; SG=subgroups; Umol/l=micromole per liter

Evidence Table 21. Summary of other outcomes reported in studies of statins plus IV fluids versus IV fluids with or without placebo for the prevention of contrast-induced nephropathy

Author, yr	Comparisons	Mortality, n/N (%)	Need for RRT, n/N (%)	Other events, n/N (%)
Han, 2013[32]	Arm 1: IV normal saline Arm 2: Rosuvastatin + IV normal saline	At 30 days, all cause: 5/1500 (.3) 3/1498 (.2) P=0.73	At 30 days: 2/ 1500 (0.1) 0/1498 P=0.5	Worsening heart failure: 64/1500 (4.3) 39/1498 (2.6) P=0.02
Jo, 2008[39]	Arm 1:Placebo + 0.45% saline Arm 2: simvastatin + 0.45% saline		At 3 days: 1/118 (.8) 0/118 P=NR[f]	Length of stay: 5.1 days 4.5 days P=0.39 Composite outcome: 5/123 (4.1) 3/124 (2.4) P=0.498[c]
Li, 2012 [50]	Arm 1: Placebo + IV normal saline Arm 2: Atorvastatin + IV normal saline	NR	NR	Elevated ALT: NR (1.2) NR (3.85) P=0.57
Ozhan, 2010[63]	Arm 2: NAC + IV normal saline Arm 3: NAC + Atorvastatin +IV normal saline	NR	NR	NR
Patti, 2011[64]	Arm 1: Placebo Arm 2: Atorvastatin	NR	NR	Length of stay:[b] 3.2 +/-.8 days 2.9 +/-.9 days P=0.007 Acute renal failure 1/121 (0.8) 0/120 (0) P=nr
Quintavalle, 2012[66]	Arm 2: NAC+ IV $NaHCO_3$ Arm 3: Atorvastatin + NAC + IV $NaHCO_3$	At 1 year, whole population: 29/402(7)	At 1 year, whole population: 8/402(2)	Majpr adverse events (not defined) At 24 hours post procedure 9/45 (20) patients with CIAKI 28/357 (7.8) patients without CIAKI
Toso, 2010[77]	Arm 1: Placebo + IV normal saline + NAC Arm 2: atorvastatin + IV normal saline + NAC	0/152 (0) 1/152 (0.6) P=NR	1/152 (0.6) 0/152 (0) P=NR[f]	NR
Xinwei, 2009[82]	Arm 2: Simvastatin 20mg + IV normal saline Arm 3: Simvastatin 80mg + IV normal saline	NR	NR	Acute renal failure at 24 hours: 1/115 0/113 P=NR

Evidence Table 21. Summary of other outcomes reported in studies of statins plus IV fluids versus IV fluids with or without placebo for the prevention of contrast-induced nephropathy (continued)

%=percent; ALT=alanine aminotransferase; CIN=contrast induced nephropathy; Mg/dl=milligram per deciliter; Mg=milligram; Cr= creatinine; N=sample size; NAC=N-acetylcysteine; NaHCo3=sodium bicarbonate; NR=not reported; NS=normal saline; P=p-value; RRT=renal replacement therapy; vs.=versus

* p values associated with chi square tests unless otherwise specified
† Specific error estimation, mean (standard error) vs. mean (standard deviation), not reported
‡ Fisher's exact
§ Multiple comparisons (% placebo vs. % simvastatin) reported: non diabetes, (1.1 vs. 1.2, p value=1.0); Dose of CM≥140 ml, (6.0 vs. 1.7, p value=.369); dose of CM< 140ml, (0 vs. 4.1, p value=.498); LVEF≤40 ml, (2 vs. 0, p value=.476); LVEF>40%(18.2 vs. 0, p value=1.0); Age≥75 years, (6.3 vs. 6.3, p value=1.0); Age < 75 y, (2.9 vs. 2.0, p value=.068)
¶ Composite outcome of death, myocardial infarction, revascularization, cerebral infarction, and dialysis [c]defined as NYHA classification (class change ≥1)
‖ Fisher's exact calculated as p value=1.0 for both comparisons
n/N refers to number of events divided by number at risk.

Evidence Table 22. Reported adverse events in studies comparing statins plus IV fluids versus IV fluids with or without placebo for the prevention of contrast-induced nephropathy

Author, Year	Adverse events
XinWei, 2010[82]	Postprocedureal acute renal failure defined as a rapid decrease in renal glomerular filtration with a >176.8 umol/L (2 mg/dl)creatinine increase from baseline. No postprocedural acute renal failure occurred in the S80 group compared with 1 case of renal failure in the S20 group at 24 hours after PCI.

Evidence Table 23. Summary of studies comparing adenosine antagonists versus other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparisons	N	Population	Age, Range of means§	No. female (%)‡	Mean followup	CM route	Definition of CIN*	Study limitations†
Baskurt, 2009[9]	IV normal saline vs NAC + IV normal saline vs NAC + theophylline + IV normal saline	217	Moderate CKD: eGFR 30-60 ml/min	67.1-67.9	87 (67)	48 hour (short term)	LOCM Ioversol IA	A2	H
Bilasy, 2012[10]	IV normal saline vs theophylline + IV normal saline	60	At least moderate risk for CIN (defined by the Mehran risk score)	56.8-57.2	24 (40)	72 hours	LOCM Iopamidol IA	A3	L
Demir, 2008[22]	IV normal saline vs NAC + IV normal saline vs misopristol + IV normal saline vs theophylline + IV normal saline vs nifedipine + IV normal saline	97	General (non-diabetic)	24-85	43 (45)	Within 3 days	LOCM Iomeprol, Iopamidol IV	A2	H
Kinbara, 2010[45]	IV normal saline vs aminophylline + IV normal saline vs NAC + IV normal saline	45	Stable coronary artery disease	70-71	17 (37)	48 hours	LOCM Iopamidol IA	A2	M
Matejka, 2010[56]	IV normal saline vs theophylline + IV normal saline (all participants had unrestricted oral fluid intake)	56	Cr >1.47mg/dl	75	22 (39)	48 hours CIN 86 hours SrCr	LOCM Iodixanol IA	A3	M

%=percent; CIN=contrast induced nephropathy; CKD=chronic kidney disease; CM=contrast media; F=female; IA=Intrartieral; IOCM=iso-osmolar contrast media; IV=intravenous; LOCM=low osmolar contrast media; mg/dl=milligram per deciliter; N=sample size; NAC=N-acetylcysteine; NS=normal saline; vs.=versus; Cr=creatinine

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Percent females in entire study population
§ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table 24. Contrast induced nephropathy outcomes in a study comparing adenosine agonists versus other interventions for the prevention of contrast induced nephropathy and other outcomes that is not included in the meta-analysis

Author, year	Measure	SG	Intervention	Arm	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison* statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Baskurt, 2009[9]	Creatinine		IV normal saline Hydration	1	48 hours	72	5 (6.9)	All arms p=0.033				
Baskurt, 2009[9]	Creatinine		IV normal saline Hydration + N-acetylcysteine	2		73	7 (9.6)					
Baskurt, 2009[9]	Creatinine		IV normal saline Hydration + N-acetylcysteine + theophylline	3		72	0 (0)					

Evidence Table 25. Summary of all outcomes reported in studies using adenosine antagonists versus other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparisons	Mortality (in hospital) n/N(%)	Need for RRT n/N(%)‖	Other events n/N(%)
Baskurt, 2009[9]	Arm 1: IV normal saline Arm 2: NAC + IV normal saline Arm 3: NAC + theophylline + IV normal saline	0 (-)	0 (-)	0 (-)
Bilasy, 2012[10]	Arm 1: IV normal saline Arm 2: theophylline + IV normal saline	NR	NR	Cardiac death: 0 (-) Myocardial infarction: 0 (-)
Demir, 2008[22]	Arm 1: IV normal saline Arm 2: NAC + IV normal saline Arm 3: Misopristol + IV normal saline Arm 4: Theophylline + IV normal saline Arm 5: Nifedipine + IV normal saline	NR	0 (-)	Prolonged hospitalization due to azotemia: 0 (-)
Kinbara, 2010[45]	Arm 1: IV normal saline Arm 2: Aminophylline + IV normal saline Arm 3: NAC + IV normal saline	NR	NR	NR
Matejka, 2010[56]	Arm 1:IV NS Arm 2: theophylline + IV normal saline	0 (-)	0 (-)	Drug side effect: 0 (-) Worsening heart failure requiring IV diuretic : ¶ 3/56 (5.3)

%=percent; CIN=contrast induced nephropathy; N=sample size; NAC=N-acetylcysteine; NR=not reported; NS=normal saline; RRT=renal replacement therapy; vs.=versus

* p values associated with chi square tests unless otherwise specified
†Not specified
‡Calculated chi square=12.63, 4df, Yates corrected p value =.11
§calculated Fisher's exact p value>0.99
¶outcome by intervention arm not reported
‖n/N; number of events/population at risk (patients in arm)

Evidence Table 26. Adverse events in studies comparing adenosine agonists versus other interventions for the prevention of contrast induced nephropathy and other outcomes

Author, Year	Adverse events
Baskurt, 2009[9]	no cardiac events reported
Bilasy, 2012[10]	no major cardiac events
Demir,2008[22]	no need for RRT or prolonged hospital stay
Kinbara, 2010[45]	none reported
Matejka, 2010[56]	Fluid overload: Adequate hydration was accompanied by mildly elevated LVEDP in both treatment groups (17±11 and 15±8 mmHg; p=0.43); Heart failure: Worsening heart failure requiring IV diuretic treatment during infusion therapy appeared in 3(5.3%) patients and did not require intubation and/or artificial ventilation; Anaphalaxis; Other; No patient died and no patient required temporary or permanent renal replacement therapy during the study course. No adverse events related to the study drug or side effects of it were detected.

g/kg/day=gram per kilogram per day; LVEDP=left ventricular ejection diastolic pressure; min=minute; mmHG=millimeter of mercury; NaCl=sodium chloride; NR=not reported

Evidence Table 27. Summary of studies assessing the use of hemodialysis or hemofiltration for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N	CKD stages inclusion criteria, mean/range	Age, range of means‡	Mean followup	Procedure	CM	Definition of CIN*	Study limitations†
Frank, 2003[25]	IV normal saline vs. IV normal saline + hemodialysis	17	Inclusion Cr ≥.3 mg/dl Range CrCl: 9.8-29.6 mL/min Stages 4-5	47-76	8 weeks	Coronary angiography	LOCM Iomeprol	NR	H
Lehnert, 1998[49]	IV normal saline vs IV normal saline + hemodialysis	30	Inclusion Cr >1.4 mg/dl Mean Cr: 2.4 + /- 0.16 mg/dl CrCl not given	60-63.3	14 days	Angiography (27 coronary, 2 peripheral arterial, 1 venous)	LOCM Iopentol	A2	H
Marenzi, 2003[52]	IV normal saline vs. hemofiltration	114	Inclusion Cr >2.0 mg/dl Mean CrCl: 26 + /- 9 ml/min Stages 3-4	58-80	12 months	Elective coronary interventions	LOCM Iopentol	A1	H
Marenzi, 2006[54]	IV normal saline vs. hemofiltration post CM + IV normal saline vs. hemofiltration pre/post CM + IV normal saline	92	Inclusion CrCl ≤ 30 mL/min Range CrCl: 14-30 mL/min Stages 4-5	71-72	21 days	Elective diagnostic and therapeutic coronary interventions	LOCM Iopentol	A2	M
Reinecke, 2007[68]	IV normal saline + glucose vs. IV normal saline + glucose + hemodialysis vs. IV normal saline + glucose + NAC	424	Inclusion Cr ≥1.3 mg/dl and ≤ 3.5 mg/dl Median GFR 46.6 and 49.3 Stage 3	66-67.9	Median 553 Days Range 63-1316 days)	Elective left heart catheterization	LOCM Iopromide	A2	H
Vogt, 2001[80]	Saline (not specified) vs. Saline (not specified) + hemodialysis	113	Inclusion Cr >2.3 mg/dl Range CrCl: 13-30 mL/min Stages 4-5	59-80	NR	Renal angioplasty Peripheral angioplasty Coronary angiography Computed tomography	LOCM	A3	H

CKD=Chronic Kidney Disease; CM=contrast media, CIN=contrast induced nephropathy; Cr=creatinine; CrCl=creatinine clearance; IV=intravenous; LOCM=low-osmolar contrast media; NAC=N-acetylcysteine; NR=not reported; PCI=Percutaneous coronary intervention; RCT=Randomized Controlled Trial

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table 28. Contrast-induced nephropathy outcomes in a study comparing renal replacement therapy versus other interventions for the prevention of contrast-induced nephropathy nephropathy and other outcomes that is not included in the meta-analysis

Author, year	Measure	SG	Intervention	ARM	Time Point 1	Time point 1 N analyzed	n (%) with outcome at time point 1	Comparison * statistics at time point 1	Time Point 2	Time point 2 N anlyzed	n (%) with outcome at timepoint 2	Comparison statistics at time point 2
Frank, 2003[25]	Differences in changes in CrCl in both groups reported as non significant, no numbers given											
Marenzi, 2003[52] Should be with RRT	12-month mortality		Saline	1	12 months	48	9 (cumulative 1-year mortality: 30%)	p=0.1				
Marenzi, 2003[52]	12-month mortality		Hemofiltration	2		57	5 (cumulative 1-year mortality: 10%)					
Marenzi, 2006[54]	greater than 25% increase in Cr from baseline		isotonic saline	1	9 days	30	12 (40)	All arms p=0.013				
Marenzi, 2006[54] (continued)	greater than 25% increase in Cr from baseline		isotonic saline + hemofiltration post contrast	2		31	8 (26)					
Marenzi, 2006[54]	greater than 25% increase in Cr from baseline		isotonic saline + hemofiltration pre and post contrast	3		31	1 (3)					

%=percent; A1=arm 1; A2=arm 2; A3=arm 3; BL=blood level; CI=confidence interval; CIN=contrast induced nephropathy; CKD=chronic kidney disease; Cr=creatinine; GFR=glomerular filtration rate; H=hour; Mg/dl=milligram per deciliter; N=sample size; NAC=N-acetylcysteine; NS=non-significant; OR=odds ratio; P=p-value; SCr=serum creatinine; Umol/l=micromole per liter

Evidence Table 29. Summary of all outcomes reported on use of hemodialysis or hemofiltration for the prevention of contrast-induced nephropathy

Author, year	Comparison	Mortality n/N (%)	Need for RRT n/N (%)	Other events n/N (%)
Frank, 2003[25]	Arm 1: IV normal saline Arm 2: IV normal saline + hemodialysis	NR	Long-term Arm1: 1 (10%) (pulmonary edema) Arm2: 1 (10%) (uremic pericarditis) P=1.0	Pulmonary edema at 6 hours Arm1: 1 (10%) Arm2: 0 (-) P=NS
Lehnert, 1998[49]	Arm 1: IV normal saline Arm 2: IV normal saline + hemodialysis	NR	NR	NR
Marenzi, 2003[52]	Arm 1: IV normal saline Arm 2: hemofiltration	In-hospital mortality Arm1: 8 (14%) Arm2: 1 (2%) P=0.02	Emergency HD Arm1: 10 (18%) Arm2: 0 (-) P< 0.001 Long-term Arm1: 14 (25%) Arm2: 2 (3%) P<0.001	MI Arm1: 3 (5%) Arm2: 1 (2%) P=0.36 Pulmonary edema Arm1: 6 (11%) Arm2: 0 (-) P=0.02
Marenzi, 2006[54]	Arm 1: IV normal saline Arm 2: IV normal saline + hemofiltration post CM Arm 3: IV normal saline + hemofiltration pre/post CM	In-hospital mortality	Arm1: 9 (30%) Arm2: 3 (10%) Arm3: 0 (-) P=0.002	NR

Evidence Table 29. Summary of all outcomes reported on use of hemodialysis or hemofiltration for the prevention of contrast-induced nephropathy

Author, year	Comparison	Mortality n/N (%)	Need for RRT n/N (%)	Other events n/N (%)
Reinecke, 2007[68]	Arm 1: IV normal saline + glucose Arm 2: IV normal saline + glucose + hemodialysis + Arm 3: IV normal saline+ glucose + NAC	In-hospital mortality Arm1: 1 (0.7%) Arm2: 3 (2.2%) Arm 3: 1 (0.7%) P=0.427 30-day mortality Arm1: 3 (2.2%) Arm2: 3 (2.2%) Arm 3: 1 (0.7%) P=0.540 Long-term mortality (deaths per 100 patient-years) Arm1: 9.7 Arm 2: 13.1 Arm 3: 9.9 P=0.582	In-hospital Arm1: 1 (0.7%) Arm2: 2 (1.5%) Arm 3: 1 (0.7%) P=0.762	Hematomas Arm1: 1 (0.7%) Arm 2: 5 (3.7%) Arm 3: 5 (3.6%) P=0.226
Vogt, 2001[80]	Arm 1: Saline (not specified) Arm 2: Saline (not specified) + hemodialysis	Arm1: 1 (2%) Arm2: 1 (2%) P=1.0 Time of death=NS	Before day 6 Arm1: 3 (5%) Arm2: 8 (15%) P=0.12 Before day 6 Arm1: 2 (4%) Arm2: 4 (7%) P=0.44	MI Arm1: 2 (4%) Arm2: 2 (4%) P=1.0 Stroke Arm1: 0 (-) Arm2: 2 (4%) P=0.24 Pulmonary edema Arm1: 4 (7%) Arm2: 1 (2%) P=0.36

CM=contrast media; CrCl=creatinine clearance; HD-hemodialysis; HF=hemofiltration; IV=intravenous; MI=myocardial infarction; NAC=N-acetylcysteine; NS=not significant; RRT=renal replacement therapy

*n/N; number of events/population at risk (patients in arm)

Evidence Table 30. Adverse events in studies comparing replacement therapy versus other interventions for the prevention of contrast-induced nephropathy

Author, Year	Adverse events
Frank, 2003[25]	Fluid overload: One participant in the control group developed respiratory insufficiency with pulmonary edema 6 hours after angiography and needed artificial ventilation for 30 hours.; Heart failure; Anaphalaxis; development of ESRD: One patient in each group developed ESRD at 8 weeks.; oliguria or anuria: No patient in either group developed these conditions at 1 week. One participant in each group underwent coronary artery bypass surgery; both were anuric after the cardiac surgery.
Marenzi, 2003[52]	pulmonary edema:6 in the control group0 in the HF group(P 0.02); Heart failure; Anaphalaxis; treatment associated hypotension (in text); hypotension or shock (in the table): In the text: no treatment-associated hypotension in HF group (one participant developed shock two days at the end of the hemofiltration treatment)In the table: "hypotension or shock" in 3 participants in the control group and 1 in the HF group (P 0.36); Bleeding at site of vascular access: 3 patients in the HF group Another AE: "blood transfusion required"(in table). 3 in control group and 1 in HF group (P 0.36); myocardial infarction: control group: 2 Q wave and 1 non-Q wave HF group: 1 Q wave and 1 non-Q wave (this information is in a table)Also: high-rate atrial fibrillation with hemodynamic instability1 patient in the HF group; none mentioned in the control group
Marenzi, 2006[54]	Acute myocardial infarction: 5 cases in the control group, 4 in the post hemofiltration and 1 in pre/post hemofiltration; Cardiogenic shock requiring intra-aortic balloon pump: 1 case in the control group and none in the other 2 groups; Blood transfusion: 4 cases in the control group, 6 in the post hemofiltration and 5 in pre/post hemofiltration
Reinecke,2007[68]	adverse events reported as secondary outcome.
Vogt, 2001[8080]	Table 3 lists clinical events, though most of these were actually outcomes. The additional AEs are: HD-related complications (AV formation): 2 of the 55 HD patients (4%) (none in the non-HD group). P 0.24

AE=adverse event; ESRD=end stage renal disease; HD=hemodialysis; HF=hemofiltration; NR=not reported

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Appendix F. Study Limitations

Author, Year	Was the allocation sequence adequately generated?	Was allocation adequately concealed?	Was knowledge of the allocated intervention adequately prevented during the study?	Were incomplete outcome data adequately addressed?	Are reports of the study free of suggestion of selective outcome reporting?	Study limitations
ACT, 2011[1]	Yes	Yes	Yes	Yes	Yes	Low
Alioglu, 2013[2]	No	No	Yes	Unclear	Yes	Moderate
Allaqaband, 2002[3]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Amini, 2009[4]	Yes	Yes	Yes	Unclear	Yes	Low
Aslanger, 2012[5]	Yes	No	No	Yes	Yes	High
Awal, 2011[6]	Unclear	Unclear	Unclear	Yes	Yes	High
Azmus, 2005[7]	Yes	Yes	Yes	Yes	Yes	Low
Baker, 2003[8]	Unclear	Unclear	Yes	Yes	Yes	Low
Baskurt, 2009[9]	Unclear	Unclear	Unclear	Yes	Yes	High
Bilasy, 2012[10]	Yes	Yes	Yes	Yes	Yes	Low
Boccalandro, 2003[11]	Unclear	Unclear	Unclear	Unclear	Yes	High
Boucek, 2013[12]	Yes	Yes	Yes	Yes	Yes	Low
Brar, 2008[13]	Yes	Yes	Yes	Yes	Yes	Low
Briguori, 2002[14]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Brueck, 2013[15]	Yes	Yes	Yes	Yes	Yes	Low
Burns, 2010[16]	Yes	Yes	Unclear	Yes	Yes	Moderate
Carbonell, 2010[17]	Yes	Yes	Yes	Yes	Yes	Low
Castini, 2010[18]	Yes	Yes	Yes	Unclear	Yes	Low
Chousterman, 2011[19]	No	No	No	Yes	Yes	High
Chousterman, 2013[20]	No	No	No	Yes	Yes	High
Demir, 2008[21]	No	Unclear	No	No	No	High
Durham, 2002[22]	Yes	Unclear	Unclear	Yes	Yes	Moderate

Author, Year	Was the allocation sequence adequately generated?	Was allocation adequately concealed?	Was knowledge of the allocated intervention adequately prevented during the study?	Were incomplete outcome data adequately addressed?	Are reports of the study free of suggestion of selective outcome reporting?	Study limitations
Dussol, 2006[23]	Yes	Yes	No	Yes	No	Moderate
Ferrario, 2009[24]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Frank, 2003[25]	No	No	No	Unclear	No	High
Fung, 2004[26]	Yes	Yes	No	Yes	Unclear	High
Gomes, 2012[27]	Yes	Unclear	Unclear	Unclear	Yes	High
Gulel,2005[28]	Yes	No	Unclear	Yes	Yes	Moderate
Gunebakmaz, 2012[29]	Unclear	Unclear	Unclear	Yes	Yes	High
Han, 2013[30]	Yes	No	No	No	No	High
Heguilen, 2013[31]	Unclear	Unclear	Yes	Yes	Yes	Moderate
Holscher, 2008[32]	Unclear	Unclear	Unclear	Yes	Yes	High
Hsu, 2007[33]	Yes	Unclear	Yes	Yes	Yes	Moderate
Hsu, 2012[34]	No	No	No	Yes	Yes	High
Izani Wan Mohamed, 2008[35]	Yes	Yes	Yes	Yes	Yes	Low
Jaffery, 2012[36]	Unclear	Unclear	Unclear	Yes	Yes	High
Jo, 2008[37]	Yes	Yes	Yes	Unclear	Yes	Low
Kay, 2003[38]	Yes	Yes	Unclear	Yes	Yes	Moderate
Kefer, 2003[39]	Yes	Yes	Yes	Yes	Yes	Low
Khalili, 2006[40]	Unclear	Unclear	Unclear	Unclear	Yes	High
Kim, 2010[41]	Yes	Unclear	No	Yes	Yes	Moderate
Kimmel, 2008[42]	Unclear	Unclear	Yes	Yes	Yes	Moderate
Kinbara, 2010[43]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Koc, 2013[44]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Kotlyar, 2005[45]	Yes	Unclear	Yes	Yes	Unclear	High
Lee, 2011[46]	Yes	Yes	No	Yes	Yes	Moderate
Lehnert, 1998[47]	Unclear	Unclear	No	Unclear	Unclear	High

Author, Year	Was the allocation sequence adequately generated?	Was allocation adequately concealed?	Was knowledge of the allocated intervention adequately prevented during the study?	Were incomplete outcome data adequately addressed?	Are reports of the study free of suggestion of selective outcome reporting?	Study limitations
Li, 2012[48]	Unclear	Unclear	Yes	Yes	Yes	Moderate
MacNeill, 2003[49]	Unclear	Unclear	Yes	Unclear	No	High
Marenzi, 2003[50]	Yes	Unclear	No	Unclear	Unclear	High
Marenzi, 2006[51]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Marenzi, 2006[52]	Yes	Yes	Unclear	Yes	Yes	Moderate
Masuda, 2007[53]	Yes	Yes	Yes	No	Yes	Low
Matejka, 2010[54]	Yes	Yes	Yes	No	No	Moderate
Merten, 2004[55]	Yes	Unclear	Yes	Yes	Yes	Moderate
Miner, 2004[56]	Unclear	Unclear	Unclear	Yes	Yes	High
Motohiro, 2011[57]	Unclear	Yes	Yes	Yes	Yes	Moderate
Ochoa, 2004[58]	Unclear	Unclear	Yes	Yes	Yes	High
Oldemeyer, 2003[59]	Yes	Yes	Yes	Yes	Yes	Low
Ozcan, 2007[60]	Unclear	Unclear	Unclear	Yes	Yes	High
Ozhan, 2010[61]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Patti, 2011[62]	Yes	Yes	Yes	Yes	Yes	Low
Poletti, 2007[63]	Yes	Yes	Yes	Yes	Yes	Low
Quintavalle, 2012[64]	Yes	No	No	Yes	Yes	Moderate
Ratcliffe, 2009[65]	Unclear	Unclear	Unclear	Yes	Yes	High
Recio-Mayoral,2007[66]	Unclear	No	No	Yes	Yes	High
Reed, 2010[67]	No	No	No	Yes	Yes	High
Reinecke, 2007[68]	Unclear	Unclear	Unclear	Yes	Yes	High
Sadat, 2011[69]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Sandhu, 2006[70]	Yes	Yes	Unclear	Yes	Yes	Moderate
Seyon, 2007[71]	No	No	No	No	Yes	High
Shavit, 2009[72]	No	No	Yes	No	Yes	High
Shyu, 2002[73]	Yes	Yes	Yes	Yes	Yes	Low

Author, Year	Was the allocation sequence adequately generated?	Was allocation adequately concealed?	Was knowledge of the allocated intervention adequately prevented during the study?	Were incomplete outcome data adequately addressed?	Are reports of the study free of suggestion of selective outcome reporting?	Study limitations
Tanaka, 2011[74]	No	Unclear	Unclear	Yes	Yes	High
Tepel, 2000[75]	No	No	No	Yes	Yes	High
Thiele, 2010[76]	Yes	No	Unclear	Yes	Yes	Moderate
Toso, 2010[77]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Ueda, 2011[78]	Yes	Unclear	Unclear	Yes	Yes	Moderate
Vasheghani-Farahani, 2010[79]	Yes	Yes	Yes	Yes	Yes	Low
Vogt, 2001[80]	No	No	No	No	Unclear	High
Webb, 2004[81]	Yes	Yes	Yes	Yes	Yes	Low
Xinwei, 2009[82]	Yes	No	No	Yes	Yes	Moderate

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Appendix G. Strength of Evidence

Outcome	Study design: No. studies (N)	Study limitations	Directness	Consistency	Precision	Strength of evidence*	Summary of key outcomes
Development of CIN short term	RCT:						
Need for RRT	RCT:						
Cardiovascular outcomes	RCT:						
Mortality	RCT:						
Adverse events	RCT:						

CIN=contrast induced nephropathy; IOCM=iso-osmolar contrast medium; LOCM= low-osmolar contrast medium; NA=not assessed; RCT=randomized controlled trial; RRT=renal replacement Therapy

* Due to heterogeneity in the study limitations across studies
the median study limitation value was chosen when distribution across studies was normal. In the instance where there is a split between study limitation scores the more conservative study limitation designation was chosen.
†H(7), M(11), L(7)
‡L(1), M(3), H(1)
§ L(3), M(3), H (0)
¶ L(1), M(6), H (1)
‖L (5), M (6), H (1)

Appendix H. Miscellaneous Comparisons

N-acetylcysteine versus Other Interventions

Several studies examined the potential effects of N-acetylcysteine compared with various other forms of potential prophylaxis. Some of these studies were addressed in other sections, but will also be mentioned briefly here

Study Characteristics

We found twenty-three studies of N-acetylcysteine compared with other medications, intravenous (IV) fluids, and dialysis, most of which are described in other sections of this report. In this group of studies, N-acetylcysteine was compared with the following medications: ascorbic acid,[1, 2] nebivolol,[3] atorvastatin,[4] aminophylline,[5] theophylline,[6-8] fenoldopam,[9-11] and misoprostol.[7] N-acetylcysteine has also been used in various doses with and compared against IVsaline in various regimens. N-acetylcysteine also has been used with IV saline and compared with N-acetylcysteine plus IV sodium bicarbonate.[12, 13] IV saline and IV sodium bicarbonate with and without N-acetylcysteine have been compared to each other. [14, 15] Other studies compared N-acetylcysteine plus IV fluids with dialysis plus IV fluids[16] and to other variations of IV fluids,[13, 17-19] including as an arm in some of the studies that also compared N-acetylcysteine with other medications. Some studies compared two different doses of N-acetylcysteine to each other,[20-22] and one study compared IV saline plus N-acetylcysteine post-procedure with IV bicarbonate plus N-acetylcysteine pre-procedure and post-procedure [23] (Appendix I, Evidence Tables A-C; D).

The follow-up time for these studies varied between 48 hours and 1316 days; most of the studies had a follow-up time less than 5 days. The mode of contrast media administration in all studies was intra-arterial (IA), except for one study that included either IA or IV contrast media administration.[7] Studies varied in terms of: doses of N-acetylcysteine used; doses, type, and duration of IV fluids; sample size; and outcome time.

Some studies used a serum creatinine greater than 0.5 mg/dL in the definition of CIN, and some used a serum creatinine greater than 25 percent (and some used both definitions). Because of the large heterogeneity of studies, a meta-analysis was not performed. In all cases, CIN was defined as occurring at either 48 or 72 hours, but in some cases, the incidence of CIN was also presented at later time points. Castini et al did not present the 48-hour CIN data in the paper, but provided this information to us via personal communication. [18]

Regarding the quality of the 23 studies we examined in this section, nine had a high risk of bias, [3, 6, 13, 15-17, 19, 23] one had a low risk, [1] and the remaining 13 had medium risk.[2, 4, 5, 9-12, 14, 18, 20-22] All studies with high risk of bias had low scores in the following domains: reporting of allocation generation, allocation concealment, and masking of subjects and/or investigators.[3, 6, 13, 15-17, 19, 23]

Outcomes

Outcomes are presented in the evidence tables (Appendix I, Evidence Table E). Most of the studies included three treatment groups, and some of the outcomes are discussed in other sections. Some studies demonstrated a benefit of N-acetylcysteine. For example, the study by Heguilen [12] demonstrated that the use of N-acetylcysteine (given with IV sodium bicarbonate or

with IV saline) was associated with a statistically significant decrease in the occurrence of CIN when compared with IV sodium bicarbonate alone (OR 0.18, 95% CI, 0.04 to 0.72, p =0.016). In a study by Kinbara et. al., no participants receiving N-acetylcysteine with IV saline or aminophylline with IV saline developed CIN, while 26.7 percent of participants in the group receiving only IV saline developed CIN (p = 0.01 across all arms). [5] The incidence of CIN was higher in patients who received IV saline with fenoldopam (13.7%) compared with those who received IV saline with N-acetylcysteine (4.1%, p = 0.019) in one of the studies by Briguori.[10] A benefit of N-acetylcysteine was not consistent across all studies, although the comparator was not always the same in both groups.; One study compared placebo plus IV normal saline, low-dose N-acetylcysteine (600 mg IV pre-contrast media administration, with 600 mg orally twice a day for 48 hours after the contrast media administration) plus normal saline, and high-dose N-acetylcysteine (1200 mg IV pre-contrast media administration followed by 1200 mg orally twice a day for 48 hours after the contrast media administration) plus normal saline.[21] The incidence of CIN was 33 percent in the placebo plus saline group, 15 percent in the low-dose N-acetylcysteine group, and 10 percent in the high-dose N-acetylcysteine group (p < 0.001 across all groups). In a study by Briguori,[22] single-dose N-acetylcysteine (600 mg orally twice daily on the day before and day of contrast media administration) was also less successful than double-dose N-acetylcysteine (1200 mg orally twice daily on the day before and day of contrast media administration) at preventing CIN (11% vs 3.5%, p=0.38) (Appendix I, Evidence Table E).

In some studies, the comparator between groups was not N-acetylcysteine, but rather the type or presence of IV fluids. For example, Chen, et al.[17] evaluated the effects of N-acetylcysteine with and without IV 0.45 percent saline in patients with serum creatinine greater than 1.5 mg/dL. There was a higher incidence of CIN in the group that did not receive IV fluids (34% vs 21%, p < 0.01). This was the only study of the 23 that used a comparator of no fluids and no medication. Briguori, et al.[2] found that patients receiving IV sodium bicarbonate with N-acetylcysteine were less likely to develop CIN compared with those receiving N-acetylcysteine with IV saline or N-acetylcysteine with IV sodium bicarbonate (p=0.010). In a study by Reinecke et. al, dialysis was also used as a comparator;patients receiving IV fluids with dialysis for unclear reasons were more likely to develop CIN than patients receiving IV fluids with N-acetylcysteine or IV fluids alone (0.008 across groups).[15] However, the authors of that study did demonstrate that after 30–60 days, most patients who had originally developed CIN had recovered even after undergoing hemodialysis. In addition, the percentage of patients with elevated serum creatinine concentrations at 30-60 days was similar in all treatment arms.

Finally, one of these studies compared the timing of N-acetylcysteine delivery. This study determined that IV saline with N-acetylcysteine plus IV normal saline post-procedure was less effective than IV sodium bicarbonate with N-acetylcysteine pre- and post-procedure (21.8% vs 1.8%, p= 0.0009) (Appendix I, Evidence Table E). [23] However, the fact that a different type of IV fluid was used in each group makes the results difficult to interpret.

In summary, when N-acetylcysteine was compared with interventions other than placebo or usual care, the strength of evidence was insufficient to support an overall conclusion because the studies varied too much in the comparisons and results. However, two studies provided direct evidence that a high dose of N-acetylcysteine was more effective than a low dose.

Sodium Bicarbonate versus Other Interventions

Several studies compared the effects of IV sodium bicarbonate with various other forms of potential prophylaxis. Some of these studies are addressed in other sections, but are also mentioned briefly here.

Study Characteristics

We found five studies assessing the effectiveness of IV sodium bicarbonate in preventing CIN compared with regimens not involving use of N-acetylcysteine.[24-28] All were RCTs published from 2008 to 2010. The follow-up period in these studies ranged from 48 hours to 7 days. Three of the studies included only patients with renal impairment (Appendix I, Evidence Tables A-C; F).[24, 26, 28]

The comparison interventions included acetazolamide,[27] long-term versus short-term IV sodium bicarbonate,[24] IV sodium bicarbonate in five percent dextrose versus IV saline in five percent dextrose,[28] IV sodium bicarbonate versus oral sodium bicarbonate,[25] and IV saline versus IV saline plus sodium bicarbonate.[26] Two studies used IOCM, two used LOCM, and one used both LOCM and IOCM (Appendix I, Evidence Tables A-C; F).

In most of these studies, CIN was defined as an increase in serum creatinine of at least 25 percent or at least 0.50 mg from the baseline within 48 to 72 hours.. Other outcomes assessed in this study included: duration of hospitalization,[25] need for renal replacement therapy,[26] adverse cardiac events,[27] and mortality.[25]

All five of the studies addressing the efficacy of sodium bicarbonate compared with non-N-acetylcysteine based regimens had a medium risk of bias. These studies had low scores in regards to allocation sequence generation[27], allocation concealment [24, 25, 27-29], and masking of intervention[24-26, 29]. (Appendix I, Evidence Tables A-C; F).

Contrast Induced Nephropathy

When short- and long-term sodium bicarbonate were compared in the results of these studies, neither a clinically nor statistically significant reduction in CIN was reached (RR 1.09: 95% CI, .4 to 3.1).When comparing IV versus oral fluid regimens with normal saline or bicarbonate, we saw that patients on IV saline had higher rates of CIN, but the route of administration was not associated with a clinically important or statistically significant difference.[25]

The combination of normal saline and sodium bicarbonate was both statistically and clinically superior to saline alone with patients in the combination arm having less CIN than those receiving only saline (1.4% versus 12.5%, p = 0.017).[26] Likewise, sodium bicarbonate combined with five percent dextrose was substantially better than normal saline alone in preventing CIN, but only slightly better than acetazolamide, (4.2 percent versus 16.6 percent versus 5.3%; p = 0.04 for the 3-way comparison).[27] However, when the combination of sodium bicarbonate and five percent dextrose was compared with the combination of saline and five percent dextrose, the observed difference in the incidence of CIN was not statistically significant (2.7% vs 4.2%, p=0.614) [28] (Appendix I, Evidence Table G). [27] The strength of evidence was insufficient to support a conclusion about whether sodium bicarbonate lowers the risk of CIN compared with other interventions not using N-acetylcysteine, because the studies and comparators varied too much, the effects of sodium bicarbonate were inconsistent and imprecise, the magnitude of effect was weak, and the study limitations were moderate.

Other Outcomes

None of the studies reported on mortality, adverse cardiac events, or need for renal replacement therapy. Only one study reported on duration of hospitalization [25] and they did not find a significant difference between arms (mean stay +/- 4 days for all arms). (Appendix I, Evidence Table G).

N-acetylcysteine plus Sodium Bicarbonate versus Other Interventions

A combination of sodium bicarbonate and N-acetylcysteine may help reduce CIN. The sodium bicarbonate expands the intravascular volume and may also offer protection against free radicals by alkalinization, and it has been proposed that the N-acetylcysteine may prevent vasoconstriction and the generation of free radicals.

Study characteristics

We found seven studies that assessed the effectiveness of a combined regimen of N-acetylcysteine and sodium bicarbonate (sodium bicarbonate) to prevent CIN.[2, 12, 13, 30-33] Most of the studies were RCTs with a follow-up between 48 hours and one month, except for the study by Staniloae, et al., which was a nonrandomized controlled trial. [33] The study population for all trials was comprised of patients with renal dysfunction who were undergoing coronary interventions or another major arteriographic procedure, and three of the studies only included patients with Stage 3 to Stage 4 CKD.[12, 30, 31] The studies were published from 2007 to 2013, (Appendix I, Evidence Tables A-C; H)

Some studies in this group compared N-acetylcysteine plus sodium bicarbonate against a combination of saline and N-acetylcysteine.[2, 32] One study compared N-acetylcysteine plus sodium bicarbonate to RenalGuard (furosemide plus saline plus N-acetylcysteine).[30] Another study comparesd N-acetylcysteine plus sodium bicarbonate to a placebo plus sodium bicarbonate.[31] Three other studies compared N-acetylcysteine plus sodium bicarbonate to only sodium bicarbonate.[12, 13, 33]

In all studies, sodium bicarbonate was given intravenously at 3 ml/kg/hour or at 1 ml/kg/hour, before and after contrast media administration. A total of two doses of N-acetylcysteine were given prior to and after contrast media administration. Most of the studies used nonionic, iso-osmolar contrast media (IOCM), except for Heguilen et al which used nonionic low-osmolar contrast (LOCM).[12] Two studies also included administration of LOCM.[31, 33] The main outcome of the trials was CIN, which was defined in most studies as an increase in serum creatinine of at least 25 percent or greater than 0.5 mg/44µmol/L increase from baseline in 48 to 72 hours. In one study, CIN was assessed within five days and again after 48 hours.[32] Another study used an increase in serum creatinine of 0.3 mg/dl from baseline at 48 hours as the definition of CIN, and they reported an increase in serum creatinine as a secondary end point.[30] Secondary outcomes included mortality,[12, 30] need for renal replacement therapy,[12, 30, 31] and adverse cardiac events[30, 31] (Appendix I, Evidence Tables A-C; H)

Regarding study quality, two studies had high risk of bias scores[13, 31]; three had medium risk of bias[2, 12, 33]; and two had low risk of bias[30, 32]. They had low scores in regards to allocation generation [2, 12, 13, 33], allocation concealment [12, 13, 31, 33], masking of intervention[13, 31], and incomplete data[31].

Contrast Induced Nephropathy

Three studies reported a statistical difference in the incidence of CIN between the combined N-acetylcysteine plus sodium bicarbonate regimen and other interventions.[2, 12, 30] The results showed that the N-acetylcysteine plus sodium bicarbonate regimen was inferior to the RenalGuard regimen clinically and statistically.[30] This was true across several CIN definitions.

Briguori, et al, Heguilen, et al, and Ratcliffe et. al. reported the potential clinical superiority of N-acetylcysteine plus sodium bicarbonate over sodium chloride plus N-acetylcysteine. [2, 12, 13] Of note, the difference found in Brigouri et. al. was both clinically and statistically significant across several CIN definitions. However, when examining the same comparisons, Maioli, et al. reported a potential clinical but not statistical superiority of sodium chloride plus N-acetylcysteine over N-acetylcysteine plus sodium bicarbonate. [32] In addition, potential clinical but not statistical differences were reported when N-acetylcysteine plus sodium bicarbonate was compared separately with a placebo plus sodium bicarbonate[31] or the combination of sodium chloride plus ascorbic acid plus n-acetylcysteine.[32] According to Heguilen, et al., N-acetylcysteine plus sodium bicarbonate reduced CIN by a clinically important margin that was not statistically significant when compared with sodium bicarbonate, but no such difference was reported by Maioli, 2008 et al.[12, 32] (Appendix I; Evidence Table I). The strength of evidence was insufficient to determine whether the addition of N-acetylcysteine to IV sodium bicarbonate decreases the risk of CIN because of medium study limitations and both inconsistency and imprecision in the effect estimates (Appendix I; Evidence Table I).

Other Outcomes

When the need for renal replacement therapy was assessed in patients receiving N-acetylcysteine plus sodium bicarbonate compared with those on the RenalGuard regimen, a difference was seen that could be clinically important, but was not statistically significant because of the small number of events.[30] Likewise, none of the studies were large enough to find a statistically significant difference in mortality, adverse cardiac events, or duration of hospitalization between N-acetylcysteine plus sodium bicarbonate and any of the interventions because of the small number of events (Appendix I; Evidence Tables I). The strength of evidence was not graded for these outcomes because so many different comparisons and outcomes were assessed.

Diuretics versus Other Interventions

Diuretics have been investigated as prophylaxis for CIN because of several proposed benefits: (1) reducing the duration of nephron exposure to the contrast media via forced dieresis; (2) protecting against medullary ischemia; and (3) allowing for increased concurrent hydration as a result of decreased concern of over hydration and pulmonary edema. However, the use of diuretics alone without concurrent hydration is shown to be detrimental because excessive diuresis is found to aggravate the hypoperfusion, vasoconstriction, and viscosity, which can lead to an increased risk of CIN.[34] As a result, we question the effectiveness of using diuretics without concurrent hydration.

Study Characteristics

We found three studies evaluating the use of different diuretics (furosemide, mannitol, and acetazolamide) in combination with intravenous (IV) saline to prevent CIN.[27, 35, 36] All studies were RCTs and included patients undergoing cardiovascular interventions. Renal function and functional status (New York Health Association classification) were not study inclusion criteria. All included patients with diabetes mellitus, although only one study reported subgroup analysis for this population.[36] Two studies used low-osmolar contrast (LOCM) and one used iso-osmolar contrast (IOCM).

The studies were published between 1994 and 2013, and all studies except one evaluated the effect of a single medication (Appendix I; Evidence Tables A-C; K).

Two studies evaluated furosemide as the diuretic of interest,[35, 36] using it as a single comparator.[35, 36] The diuretic was given IV in all of the studies, but the protocols and doses vary. One study evaluated the effects of mannitol,[36] and only one included acetazolamide.(Appendix I; Evidence Tables A-C; K).[27]

Two studies had medium risk of bias scores[27, 35], and one study had a low risk of bias score.[36] The medium risk of bias scores were in regards to inadequately described allocation generation[27]and allocation concealment [27, 35].

Contrast Induced Nephropathy

The results on furosemide were conflicting and suggested the effects were dose-dependent. A study using a low dose of furosemide reported a clinically important protective effect against the development of CIN with a CI that did not rule out the possibility of an unimportant difference (RR 0.29, 95% CI, 0.10 to 0.85).[35] A study using a high dose of furosemide reported an increased risk of CIN (40% in the furosemide group vs 11% in the IV saline group, p = 0.02) (Appendix I; Evidence Table L).[36]

Overall, the strength of evidence was insufficient to support a conclusion about the effectiveness of furosemide in preventing CIN because the effects of diuretics were inconsistent and imprecise, the magnitude of effect was weak, and studies had medium risk of bias.

In addition, mannitol did not offer any protection against the development of CIN. When used alone, patients had higher rates of CIN than patients receiving IV saline (28% vs 11%) but less than those receiving furosemide (28% vs 40%); none of these differences were significant (Appendix I; Evidence Table L).[36]

The single study on the use of acetazolamide showed a clinically important and statistically significant benefit when compared with IV saline (5.3% vs 12.5%, p=0.04), but no difference

when compared with IV sodium bicarbonate (5.3% vs 4.2%). (Appendix I; Evidence Table L).[27]

Other Outcomes

The use of furosemide did not indicate a statistically significant difference when compared with IV saline and evaluating other clinical outcomes because of infrequent events, however the effect sizes demonstrated a potential clinical significance. Patients presented similar rates of complications and need for RRT in both groups in the studies reporting these outcomes. Overall, there was insufficient strength of evidence to support a conclusion about the effects of furosemide on other clinical outcomes. (Appendix I; Evidence Table L).[35, 36]

Vasoactive Agents versus Other Interventions

Persistent arterial vasoconstriction may lead to direct tubular toxicity, medullar ischemia, and even cellular damage. The use of vasoactive agents may antagonize the contrast media's toxic effect by increasing the flow, but the renoprotective effect can vary according to the mechanism of action of each vasodilator.[37, 38]

Study Characteristics

We found eight studies evaluating different kinds of vasoactive agents to prevent CIN. This included four studies on fenoldopam, a selective dopamine receptor agonist,[9-11, 39] two on calcium antagonists (one with nifedipine),[7] one with the combination of amlodipine and valsartan, an angiotensin receptor blocker),[40] one on benazepril (an ACE inhibitor),[41] and one on nevibolol (a beta blocker).[3]

Except for one retrospective observational cohort, all studies were RCTs.[39] Outside of one study including only patients undergoing computed tomography,[7]all studies included patients undergoing cardiovascular interventions. Renal function and functional status were not study inclusion criteria.

All studies included patients with diabetes mellitus, but only one performed subgroup analysis for this population.[10] Four studies used low-osmolar contrast (LOCM), three used iso-osmolar (IOCM), and one used both IOCM and LOCM. The studies were published between 2002 and 2013, and all had a follow up of 48 to 72 hours (Appendix I; Evidence tables A-C; M).

The studies were very heterogeneous, from the medications included to the doses used. Four compared fenoldopam with N-acetylcysteine, three compared intravenous (IV) fenoldopam versus oral N-acetylcysteine[9-11] and one compared intrarenal fenoldopam with oral N-acetylcysteine.[39] While the fenoldopam dose was similar between studies and was delivered intravenously, the N-acetylcysteine dose varied from 1200 to 4800 mg. All vasoactive agents were started before the administration of contrast media. (Appendix I; Evidence Tables A-C; M).

Five of the eight studies had a high risk of bias. In those studies, the risk of bias was high because of problems with allocation generation and concealment. Two studies also had incomplete data.

Contrast Induced Nephropathy

When fenoldopam was compared with low doses of N-acetylcysteine or IV saline, there were no differences in the incidence of CIN in the three studies.[9-11] However, when the N-acetylcysteine dose was increased and fenoldopam was given at comparable doses, a lower incidence of CIN was observed in the N-acetylcysteine arm, with a statistically significant difference at the highest dose (4800 mg; 13.7% vs 4.1%, OR 0.27, 95% CI, 0.08 to 0.85).[10] The effect was reversed when fenoldopam was given intrarenally (11.5% in the intrarenal fenoldopam group vs 30% in the no-fenoldopam control group, RR 0.38, 95% CI, 0.16 to 0.88)[39] (Appendix I; Evidence Tables N).

The use of calcium channel blockers showed conflicting results. Nifedipine seemed to be at least as effective as IV saline, but better thanN-acetylcysteine in protecting against CIN (0% in nifedipine and IV saline groups vs 5% in N-acetylcysteine group, p=NS),[7] amlodipine plus valsartan appeared to increase the risk of CIN without being statistically significant (17.8% vs 6.7%, p=0.197).[40]

Patients receiving benazepril seemed to have a lower incidence of CIN but the results were not statistically significant (3.5% vs 9.7%, p=0.506)[41] Conversely, the use of nevibolol did not show a clinically important or statistically significant difference (Appendix I; Evidence Tables N).

Overall, the strength of evidence was insufficient to support a conclusion about the effectiveness of vasoactive agents in preventing CIN. In these studies, the results were inconsistent and imprecise but direct, the magnitude of effect was weak, and the study limitations were high.

Other Outcomes

Few articles reported on secondary clinical outcomes. The studies reporting on complications did not report a statistically significant difference between arms. The numbers of complications were higher in the fenoldopam arm compared with the N-acetylcysteine arm, but they were not statistically significant, since the numbers were very low and very similar in all intervention arms. In general, the differences between vasoactive agents and their comparators were not significant, and the data were insufficient to draw any conclusions Appendix I; Evidence Tables O).

Antioxidants versus Hydration

Contrast media has a direct cytotoxic effect in the kidney as it generates the formation of reactive oxygen species. The use of antioxidants has been evaluated to assess the possibility of reducing the incidence of CIN by counteracting the damage caused by the free radicals produced.

Study Characteristics

We found five studies evaluating different antioxidant strategies for preventing CIN. The antioxidant probucol was evaluated in two of these studies,[42, 43] while the other three investigated pentoxifylline, an antioxidant and anti-inflammatory agent,[44] sodium-2 mercaptoethanesulfonate (MESNA), a scavenger of reactive oxygen species,[45] and zinc, which has the potential to act as an "endogenous antioxidant" via increasing metallothionein.[46] All were conducted in patients with impaired renal function (serum creatinine greater than 1.2 and less than 3.0 mg/dl) receiving low-osmolar contrast (LOCM), three studies included patients undergoing coronary interventions,[42, 44, 46] one study included patients undergoing both coronary and peripheral angiography[45]and one study included patients undergoing computed tomography.[7] All interventions were administered before contrast media; from three days [7] to 24 hours, [42, 44, 46] to immediately before (Appendix I; Evidence Tables: A-C; P-Q).[45]

Contrast Induced Nephropathy

The studies on antioxidants were too heterogeneous to include in a meta-analysis, but we show the study results in Figure 1. Although zinc did not prevent CIN in the study by Kimmel (one patient in the placebo group and one in the N-acetylcysteine had a rise in creatinine of ≥ 0.5mg/dl compared to two patients in the zinc group), the other studies that evaluated the effects of antioxidants demonstrated a lower incidence of CIN in the intervention arm when compared with IV saline, but not all of these results were statistically significant.

The incidence of CIN was lower in the probucol group when compared with IV saline (4.2% vs 21.3%, $p<0.01$,[43] and 7.84% vs 14.56% , $p=0.13$).[42] The results were only statistically significant in the study where probucol was given as a one-time high dose.[43] IV saline was given only after the administration of the contrast media in both of these studies.[42, 43] In one study, patients given MESNA had a lower incidence of CIN at 48 hours compared with a placebo (both groups receive volume expansion, 0% vs 14%, $p=0.005$).[45] Patients given pentoxifylline had a decreased incidence of CIN that would be clinically important, but the results were not statistically significant (8.5% vs 13.7%, $p=0.17$).[44] Three of the five studies had a high risk of bias. In those studies, the risk of bias was high because of problems with allocation generation and concealment. One study also had incomplete data and one study presented selective outcome reporting (Figure 1; Appendix I, Evidence Tables P; R).

Overall, the strength of evidence was insufficient to support a conclusion about the effectiveness of antioxidants in preventing CIN due to the heterogeneity of the studies with results that were inconsistent and imprecise but direct, with weak magnitude of effect and high study limitations.

Other Outcomes

The two studies analyzing additional outcomes reported that no patients required further renal replacement therapy, none died in the hospital, and none required prolonged hospitalization. The data was insufficient to draw any conclusions on other outcomes (Appendix I, Evidence Tables Q; S).

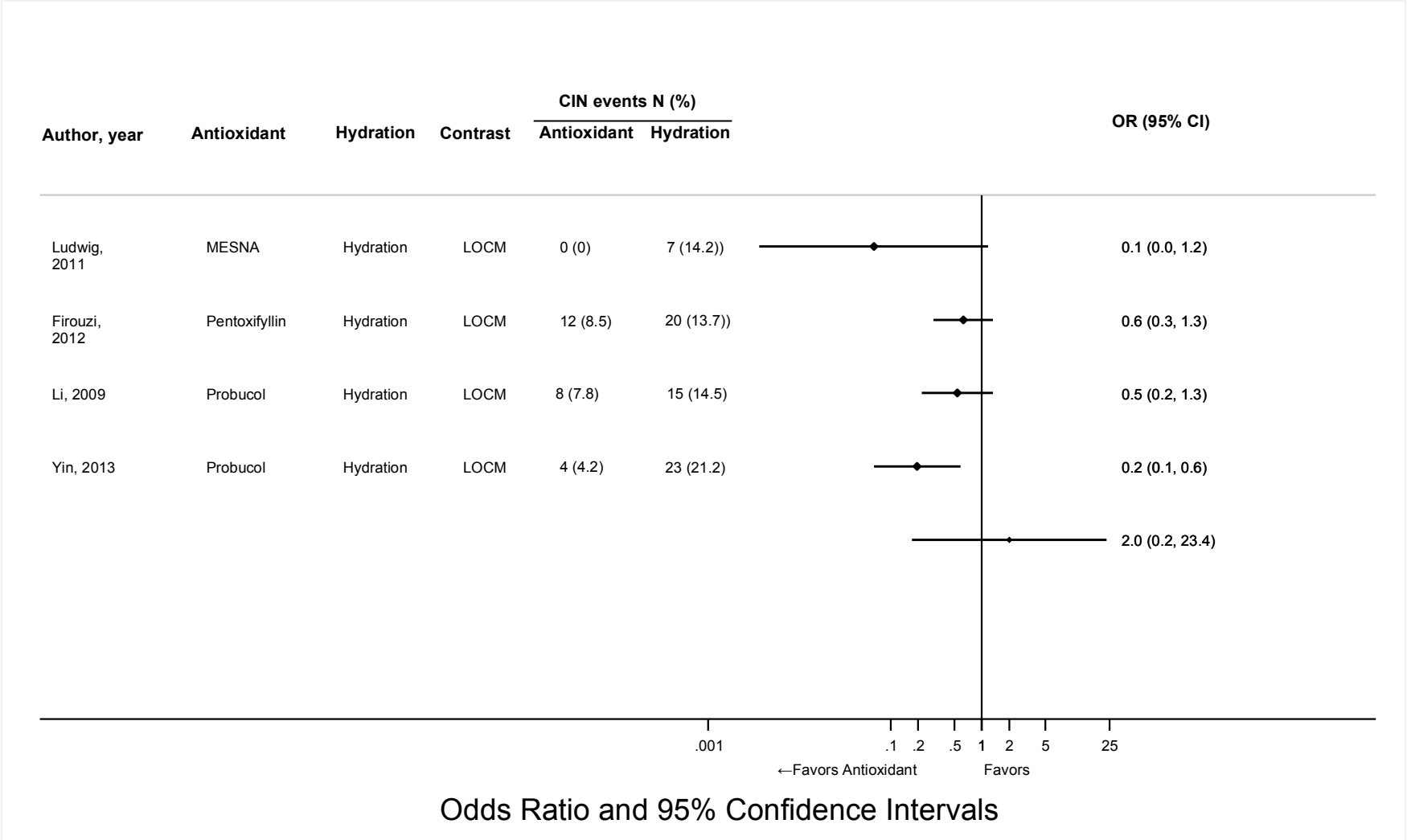
Other Comparisons

An additional study investigated misoprostol, a prostaglandin E1 analog, with another mechanism of action[7] and a study evaluated the effect of withdrawing ACE inhibitors or angiotensin receptor blockers, both of which are potentially toxic on the kidneys, before contrast media procedures.[47] The study evaluating the effects of misoprostol did not show a statistically significant effect on the incidence of CIN.

The study on therapy suspension reported a small decrease in CIN incidence when medications were withheld, but the difference was not statistically significant.[47] An important limitation of this study was that 24 hours may not be a long enough washout time for these medications(Appendix I, Evidence Tables Q; S).

Both studies had a high risk of bias. The risk of bias was high because of problems with allocation generation and concealment and they both had incomplete data.

Figure 1. Analysis of antioxidants versus hydration for the prevention of contrast induced nephropathy.



%=percent; CI=confidence interval; CIN=contrast induced nephropathy; LOCM=low-osmolar contrast media; MESNA= sodium 2-mercaptoethanesulfonate; N=sample size;

Fluids Interventions

One possible mechanism underlying CIN is hypoperfusion, which can potentially result from vasoconstriction. Based on this outcome, volume expansion with fluids, which could improve hypoperfusion, has been postulated as a possible intervention for CIN.

Study Characteristics

We found 11 studies on the use of fluids that met our inclusion criteria.[17, 25, 48-56] All 11 were RCTS and assessed the effectiveness of giving fluids to prevent CIN. The follow up period across studies ranged from 48 hours to six months (Appendix I; Evidence Tables A-C; T).

The study populations varied across studies. However, most of the studies included adults without renal impairment who were undergoing cardiovascular interventions. Three other studies included patients with some degree of renal impairment.[50, 52, 54] and two others only contained patients with acute myocardial infarction.[17, 49] The studies were published from 1999 to 2012 (Appendix I; Evidence Tables A-C; T).

Various types of fluids were compared across studies. Notably, two studies compared fluids to no fluids, with one comparing 0.45% saline[17] and the other investigating normal saline.[49] Three compared oral fluids to intravenous (IV) normal saline,[25, 48, 55] and two compared isotonic saline to hypotonic saline.[51, 56] The timing of fluid administration, whether prior to or after the procedure, was compared in two studies.[49, 53] Saline was separately compared with dextrose or sodium bicarbonate in three studies. (Appendix I; Evidence Tables A-C; T).[49, 52, 54]

In all of these studies, the intra-arterial (IA) route was the preferred route of contrast media administration; in one study, a combination of IA and IV routes was used. Seven of the studies used LOCM, three used IOCM, and two failed to report the contrast media used (Appendix I; Evidence Tables A-C; T).

All of these studies defined CIN as an increase in serum creatinine by 25 percent or a change in serum creatinine of 0.5mg from baseline at 48 or 72 hours. However, one study also used an increase of glomerular filtration rate from a baseline of 50 percent.[53]

The secondary outcomes we evaluated in these studies included mortality,[49] need for renal replacement therapy,[49, 53] length of hospitalization,[25, 54, 56] and major cardiac adverse events[49, 56] (Appendix I; Evidence Tables A-C; T).

Nine of the 11 studies had a high risk of bias. In those studies, the risk of bias was high because of problems with allocation generation and concealment, and they all also had incomplete data and selective outcome reporting.

Contrast Induced Nephropathy

In these studies, fluids given prior to contrast media administration were found to be superior to no fluids. The same was true when a stratified analysis was performed on patients with a left ejection fraction less than 40 percent.[49] However, Chen, et al. reported equivalent CIN outcomes for fluids and no fluids in patients without renal impairment, albeit with 0.45% saline. The incidence of CIN for patients who received pre- and post-contrast media fluids was similar to those only given fluids during the procedure.[48, 53] Moreover, Maioli, et al. found that normal saline given before contrast media administration was superior to normal saline after contrast media administration.(12% CIN with early fluids vs. 22.7% CIN with late fluids, p=0.001).[49]

One of the studies comparing oral fluids to IV normal saline did not find any difference in incidence of CIN,(5% incidence of CIN in both arms)[48] a second study reported different findings depending on the fluids used (22.2% CIN for IV normal saline versus 9.1% CIN of oral fluids p=0.63 and 9.5% for IV sodium bicarbonate versus 4.7% for oral sodium bicarbonate, p=0.53)[25] and another reported better outcomes for patients who received IV normal saline(2% CIN for IV saline versus 7% CIN for oral fluids).[55] Similarly, the outcomes for patients receiving hypotonic and isotonic saline were comparable. However, addition of five percent glucose to hypotonic saline was found to be inferior to isotonic saline in preventing CIN; this was especially true for women and people with diabetes mellitus (Appendix I; Evidence Tables U). [56] Overall, the strength of evidence was insufficient to support a conclusion about the effectiveness of different fluids used in preventing CIN due to the heterogeneity of the studies; different fluid regimens were compared across studies leading to the inability to assess the strength of evidence. Additionally, results were inconsistent and imprecise but direct, the magnitude of effect was weak, and the study limitations were high (Appendix I; Evidence Tables U).

Other Outcomes

None of the studies reported any statistical difference between the various fluid intervention groups by mortality, need for renal replacement therapy, duration of hospitalization stay, or adverse cardiac events. Few studies reported on these outcomes, while a few studies reported an incidence of events very similar in all arms. The data was insufficient to draw any conclusion about the comparative effects of different fluids on these other outcomes.(Appendix I; Evidence Tables U-V).

Dopamine versus Other Interventions

Increasing renal blood flow may help prevent CIN. Dopamine, a potent vasodilator, has been postulated as a possible remedy for CIN, especially among patients with impaired renal dysfunction.[57]

Study Characteristics

We found three studies assessing the effectiveness of dopamine in reducing CIN in patients with impaired renal function.[58-60] These studies were all RCTs with a follow up period of two to six days. One of the studies compared dopamine and a placebo,[60] and another compared a combination of dopamine and furosemide to a combination of dopamine, furosemide, mannitol, and saline.[59] The remaining study had three arms that compare dopamine, saline, and aminophylline.[58]

In all of the studies, published in 1998 and 1999, dopamine was administered prior to and after contrast media administration. In two of the studies, the dose of dopamine was 2.5 microgram/kg/min,[58, 60] and the other study used a dose of 3 microgram/kg/ml.[59] Contrast media administration in all of the studies was intra-arterial (IA). Two studies used LOCM[58, 60] and one used a combination of LOCM and HOCM (Appendix I; Evidence Tables A-C; W). [59]

One study had no definition set for CIN,[59] while the other studies defined CIN as a change in serum creatinine by 25 percent or greater than 0.5 mg from baseline.

These studies evaluated other outcomes, including mortality,[59] need for renal replacement therapy,[58, 59] and length of hospitalization (Appendix I; Evidence Tables A-C; W).[58]

These three studies had varying limitations, one with high risk of bias, one with medium risk of bias, and one with low risk of bias. Two of the studies had problems with allocation generation and concealment, and one study had incomplete data and selective outcome reporting.

There were a total of 213 patients in these studies. The effectiveness of dopamine in preventing CIN was comparable to giving IV saline and aminophylline. However, no statistically significant difference in CIN incidence was observed when a combination of dopamine and furosemide was compared with saline.

The addition of mannitol to the combination of dopamine and furosemide did not alter CIN outcomes. However, in a subgroup analysis of patients with serum creatinine levels above 2 mg, Hans, et al. reported the superiority of dopamine over a placebo in preventing CIN at 24 hours, 48 hours, 72 hours and 96 hours (Appendix I; Evidence Tables X).[60] The strength of evidence was insufficient to support a conclusion about the effectiveness of dopamine relative to other interventions because the studies were too heterogeneous.

Other Outcomes

No difference was observed between dopamine and any of the other treatments in terms of mortality, need for renal replacement therapy and length of hospitalization after contrast media administration. The number of events was low and comparable in all arms. Again, the strength of evidence was insufficient to support a conclusion about the effectiveness of dopamine relative to other interventions because of the heterogeneity of the studies. (Appendix I; Evidence Tables X).

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Appendix I. Evidence Tables for Miscellaneous Comparisons

Evidence Table A. Participant Characteristics for studies comparing interventions to prevent development of CIN.

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Abizaid, 1999[1]	Symptomatic coronary artery disease and renal insufficiency (SrCr ≥1.5 mg/dL)	Total		60	NR	NR	NR	NR	NR	NR	
		1	0.45% IV Normal Saline (1 ml/kg/hour) only	20		6(30)	75	NR	NR	NR	
		2	Dopamine (2.5 ug/kg/min) plus 0.45% IV Normal Saline (1 ml/kg/hour)	20		7(35)	74	NR	NR	NR	
		3	Aminophylline (4 mg/kg followed by a drip of 0.4 mg/kg/hour) plus 0.45% IV Normal Saline (1 ml/kg/hour)	20		7(35)	75	NR	NR	NR	
Acikel, 2010[2]	General: excluded CRF	Total		240	48 Hours	NR	59.8 +/- 9.7	NR	NR	NR	
		1	Control	80		29 (36.2)	60.8 +/- 10.8	NR	NR	Current: 30 (37.5)	Excluded CRF
		2	Atorvastatin	80		29 (36.2)	58.7 +/- 8.5	NR	NR	Current: 32 (40)	
		3	Chronic statins	80		30 (37.5)	59.8 +/- 9.6	NR	NR	Current: 32 (40)	
Adolph, 2008[3]	Two Cr concentration levels >106 m mol/l (>1.2mg/dl) within 12 weeks before coronary angiography	Total		145	48 hrs	32(22)	NR	NR	NR	NR	
		1	NaCl + 5% dextrose	74		14(19)	72.7+/-6.6	NR	NR	NR	
		2	NaHCO3 + 5% dextrose	71		18(27)	70.1+/-8.4	NR	NR	NR	
Alessandri, 2013[4]	Heart Disease, Ischemic heart disease	Total		296	72 Hours	NR	NR	NR	NR	NR	
		1	Sodium Chloride infusion	158		46	64.25	NR	NR	NR	
		2	sodium bicarbonate + NAC	138		46	64.25	NR	NR	NR	

Evidence Table A. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Allaqaband, 2002[5]	Creatinine ≥ 1.6 mg/dl	Total		123	48 Hours	52	71	NR	NR	NR	
		1	0.45% Saline	40		16	70	NR	NR	NR	
		2	0.45% Saline + NAC	45		17	70	NR	NR	NR	
		3	0.45% Saline + Fenoldopam	38		19	71	NR	NR	NR	
Aslanger, 2012[6]	STEMI, ST-segment elevation myocardial infarction,	Total		312	72 Hours	NR	NR	NR	NR	NR	
		1	Placebo	99		26(26)	56.1	NR	NR	NR	
Aslanger, 2012[6] (continued)		2	IV NAC	108		22(20)	56.1	NR	NR	NR	
		3	IA NAC	105		23(22)	55.9	NR	NR	NR	
Bader, 2004[7]	General	Total		39	48 Hours	NR	NR	NR	NR	NR	
		1	IV Saline infusion before and after procedure	19		3	64	NR	NR	NR	
		2	IV Saline infusion during procedure	20		4	65	NR	NR	NR	
Baskurt, 2009[8]	Moderate degree chronic kidney disease with estimated glomerular filtration rate (eGFR) between 30 and 60 mL min1.73 m2	Total		217	12 Months	87	67.4	NR	NR	NR	
		1	Hydration	72		31	67.1	NR	NR	NR	
		2	Hydration + N-acetylcysteine	73		27	67.9	NR	NR	NR	
		3	Hydration + N-acetylcysteine + theophylline	72		29	67.1	NR	NR	NR	
Briguori, 2004[9]	Impairment of renal function: serum creatinine >1.5mg/dl and/or creatinine clearance <60ml/min	Total		192	48 Hours	NR	NR	NR	NR	NR	
		2	NAC + saline	97		13(13)	68	NR	NR	NR	
		3	Fenoldopam mesylate + saline	95		16(17)	69	NR	NR	NR	

Evidence Table A. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Briguori, 2004[10]	CKD Cr >1.5 mg/dl and or creatinine clearance <60ml/min	Total		223	48 Hours	NR	NR	NR	NR	NR	
		2	NAC single dose	109		23(21)	67	NR	NR	NR	
		3	NAC double dose	114		28(16)	66	NR	NR	NR	
Briguouri, 2007[11]	CKD with stable Cr at 2.0 mg/dL and/or estimated glomerular filtration rate 40	Total		326	7 days	NR	NR	NR	NR	NR	
		1	IV Normal Saline + oral NAC	111		21 (19)	71	NR	NR	NR	
		2	IV NaHCO3 + oral NAC	108		13 (12)	70	NR	NR	NR	
		3	IV Normal Saline + IV ascorbic acid + oral NAC	107		27 (21.5)	69	NR	NR	NR	
Briguori, 2011[12]	Estimated glomerular filtration rate (eGFR)	Total		292	7 Days	NR	NR	NR	NR	NR	
		1	IV Sodium bicarbonate + oral NAC	146		43(29.5)	75	NR	NR	NR	
		2	RenalGuard: IV 0.9% saline + IV NAC + RenalGuard System + IV furosemide	146		58(39.5)	76	NR	NR	NR	
Chen, 2008[13]	Myocardial Ischemia	Total		936	6 Months	149 (16)	NR	NR	NR	NR	
		1	Normal renal function-Non hydration	330		(15)	60	NR	NR	NR	15% female refers to combined Arms 1 and 2, same with mean age 60
		2	Normal renal function-0.45% saline	330		NR	NR	NR	NR	NR	
		3	Abnormal renal function-NAC+Non hydration	188		(18)	63	NR	NR	NR	18% female refers to combined Arms 3 and 4, same with mean age 63
		4	Abnormal renal function-NAC+0.45% saline	188		NR	NR	NR	NR	NR	

Evidence Table A. ParticipantCharacteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Cho, 2010[14]	General	Total		91	NR	46 (50.5)	78 +/-8	NR	NR	NR	
		1	IV 0.9% saline	27		(37)	77 +/- 8	NR	NR	Current: 8	
		2	IV sodium bicarb + IV 0.9% saline	21		(47.6)	78 +/- 9	NR	NR	Current: 9	
		3	Oral fluids (water)	22		(55)	81 +/- 7	NR	NR	Current: 9	
		4	Oral fluids (water) + oral bicarb	21		(62)	79 +/- 2	NR	NR	Current: 7	
Demir, 2008[15]	Patients with renal insufficiency	Total		97	3 Days	43(44)	NR	NR	NR	NR	
		1	Saline	20		5(25)	58.2 +/- 11.3	NR	NR	NR	
		2	NAC + control (NAC)	20		9(45)	62.0+/- 15.8	NR	NR	NR	
		3	Misoprostol + control (M)	20		11(55)	56.5+/- 13.0	NR	NR	NR	
		4	Theophylline + control (T)	20		9(45)	56.3+/- 13.0	NR	NR	NR	
		5	Nifedipine + control (N)	17		9(53)	60.1+/- 10.7	NR	NR	NR	
Erol, 2013[16]	serum creatinine >1.1mg/dl, cardiac catheterization/intervention	Total		159	96 Hours	NR	NR	NR	NR	NR	
		1	Saline hydration	80		54(68)	65	NR	NR	Current: 21(25)	
		2	Saline hydration + allopurinol	79		61(77.5)	65	NR	NR	Current: 20(25)	
Firouzi, 2012[17]	Non-emergent coronary angiography with creatinine < 2.0 mg/dl	Total		286	48 Hours	NR	NR	NR	NR	Current: 31(21.23)	Has 544 been second reviewed?
Firouzi, 2012[17] (continued)		1	Control	146		(30.83)	57.9 (SD 10.16)	NR	NR	Current: 31(21.23)	
		2	Pentoxifylline	140		(23.58)	56.8 (SD 10.69)	NR	NR	Current: 41(29.28)	

Evidence Table A. ParticipantCharacteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Frank, 2003[18]	Patients with a known chronic renal insufficiency, not yet dialysis dependent	Total		17	NR	NR	NR	NR	NR	NR	
		1	0.9% saline volume expansion	10		1	57.6+/-12.4	NR	NR	NR	
		2	0.9% saline voume expansion + high-flux HD	7		2	66.8+/-9.2	NR	NR	NR	
Gu, 2013[19]	General	Total		859	NR	239(27.8)	NR	Other: 859(100)	NR	NR	
		1	Control--saline	437		110(25.2)	59.0+/-14; Range:	NR	NR	NR	
		2	Furosemide	422		129(30.6)	58.0+/-14; Range:	NR	NR	NR	
Gunebakmaz, 2012[20]	Coronary angiography with creatinine ≥ 1.2 mg/dl	Total		120	5 Days	NR	NR	NR	NR	NR	
		1	Saline	40		15	66.4 +/-10.7	NR	NR	NR	
		2	Saline + Nebivolol	40		11	64.1+/- 9	NR	NR	NR	
		3	Saline + NAC	40		11	64.7 +/-11.9	NR	NR	NR	
Hafiz, 2012[21]	Serum creatinine >1.6 mg/dl in non-diabetics and >1.4 mg/dl in diabetics or an estimated glomerular filtration rate (eGFR) of <50 ml/min/1.73 m2	Total		320	48 Hours	138(43.1)	Median: 73;Range: 63-80	Black: 151(47.2)	NR	NR	
		2	Normal Saline with or without NAC	161		69(42.9)	Median: 73;Range: 63-80	Black: 80(49.7)	NR	NR	
		3	Sodium Bicarbonate with or without NAC	159		69(43.4)	Median: 74;Range: 65-80	Black: 71(44.7)	NR	NR	

Evidence Table A. ParticipantCharacteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Hans, 1998[22]	Defined as SrCrof at least 1.4 mg/dL (of note, the abstract mentions the range of 1.4 to 3.5 mg/dL, but the actual inclusion seemed to be based on the SrCr of at least 1.4 mg/dL)	Total		55	4 Days	NR	NR	NR	NR	NR	
		1	Placebo	27		3	71	NR	NR	NR	
		2	Dopamine	28		3	75	NR	NR	NR	
Hashemi, 2005[23]	General	Total		88	48 Hours	NR	NR	NR	NR	NR	
		1	Placebo	46		13(28)	55.1	NR	NR	NR	
		2	Captopril	42		12(29)	55.1	NR	NR	NR	
Heguilen, 2013[24]	General	Total		0	3 Days	NR	NR	NR	NR	NR	
		2	NaHCO3 + dextrose	47		15	67.7	NR	NR	NR	
		3	NaHCO3 + NAC +dextrose	44		11	64.8	NR	NR	NR	
		4	NaCl + NAC+dextrose	42		8	69.3	NR	NR	NR	
Holscher, 2008[25]	General	Total		412	30 Days	NR	NR	NR	NR	NR	
		1	hydration only	139		68(16.5)	67.1	NR	NR	NR	
		2	hydration plus dialysis	134		58(15.5)	66.8	NR	NR	NR	
		3	hydration plus NAC	139		10(26.3)	70.5	NR	NR	NR	
Huber, 2006[26]	General	Total		91	48 Hours	31	58.5+/-14.8;Range: 21-89	NR	NR	NR	
		2	Theophylline	NR		NR	59.6	NR	NR	NR	
		3	Acetylcysteine	NR		NR	55.4	NR	NR	NR	
		4	Theophylline + Acetylcysteine	NR		NR	60.6	NR	NR	NR	

Evidence Table A. ParticipantCharacteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Kimmel, 2008[27]	Mild to moderately impaired kidney function: serum creatinine ≥ 1.2 mg/dl or a creatinine clearance < 50 ml/min	Total		54	2 Days	NR	NR	NR	NR	NR	
		1	Placebo	17		(30)	66.8	NR	NR	NR	
		2	NAC	19		(21)	71.5	NR	NR	NR	
		3	Zinc	18		(28)	67.2	NR	NR	NR	
Kinbara, 2010[28]	Stable coronary artery disease	Total		45	48 Hours	NR	NR	NR	NR	NR	
		1	Hydration	15		6 (40)	70	NR	NR	NR	
		2	Hydration and aminophylline	15		5 (33)	71	NR	NR	NR	
		3	Hydration and N-acetylcysteine	15		6 (40)	70	NR	NR	NR	
Klima, 2012[29]	>93 umol/L for women and >117 umol/L for men or estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m2	Total		258	48 Hours	92(36)	77;Range: 69-81	NR	NR	NR	
		1	0.9% saline	89		39(38)	75;Range: 70-82	NR	NR	NR	
		2	Long term sodium bicarbonate	87		30(34)	78;Range: 70-82	NR	NR	NR	
		3	Short term sodium bicarbonate	82		28(34)	75;Range: 65-81	NR	NR	NR	
Koc, 2012[30]	Serum creatinine (SCr) ≥ 1.1 mg/dL or creatinine clearance ≤ 60 mL/mi	Total		220	48 Hours	NR	NR	NR	NR	NR	
		1	IV 0.9% saline	60		14(23)	64	NR	NR	Current: 17(28)	
		2	IV NAC plus high-dose IV 0.9% saline	80		19(24)	62	NR	NR	Current: 13(17)	

Evidence Table A. ParticipantCharacteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Koc, 2012[30] (continued)		3	High-dose IV 0.9% saline	80		17(21)	65	NR	NR	Current: 15(19)	
Kong, 2012[31]	General	Total		120	6.1 Months	NR	NR	NR	NR	NR	
		1	IV 0.9% saline	40		18(45)	55.7±11.9	NR	NR	NR	
		2	Oral hydration before and after procedure	40		19(47)	57.2±9.2	NR	NR	NR	
		3	Oral hydration after procedure	40		16(40)	54.9 ± 10.8	NR	NR	NR	
Kotlyar, 2005[32]	Serum creatinine concentrations ≥0.13 mmol/l	Total		60	30 Days	NR	NR	NR	NR	NR	
		1	IV hydration	19		2(10)	69	NR	NR	NR	
		2	NAC 300mg	20		5(25)	66	NR	NR	NR	
		3	NAC 600mg	21		3(14)	67	NR	NR	NR	
Krasuski, 2003[33]	Moderate renal insufficiency with serum creatinine from 1.6mg/dl to 3mg/dL	Total		0	48 Hours	NR	NR	NR	NR	NR	
		1	overnight hydration dextrose plus saline	26		(27)	69	NR	NR	NR	
		2	Bolus normal saline	37		(11)	68	NR	NR	NR	
Lawlor, 2007[34]	Preexisting renal impairment. Stable , chronic renal insufficiency	Total		78	48 Hours	NR	NR	NR	NR	NR	Sex not specified in the entire paper. I abstracted sex as male
		1	IV Hydration	25		8(32)	NR	NR	NR	Current: 6(24)	
		2	IV Hydration + NAC	25		6(24)	NR	NR	NR	Current: 19(76)	
		3	Oral Hydration+NAC	28		10(36)	NR	NR	NR	Current: 8(28)	
Li, 2009[35]	Planned coronary angiography	Total		205	3 Days	NR	NR	NR	NR	NR	+/- SD
		1	Control	103		37	63+/-11	NR	NR	NR	
		2	Probucol	102		52	62+/-11	NR	NR	NR	

Evidence Table A. ParticipantCharacteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Li, 2011[36]	Mild and/or moderate renal insufficiency: ≥60 to ≤89 ml·min^-1·1.73 m^-2 and ≥30 to ≤59 ml·min^-1·1.73 m^-2 in eGFR	Total		114	72 Hours	NR	NR	NR	NR	NR	
		1	Control	62		27(44)	61.8 +/- 9.4	NR	NR	NR	
		2	Benazepril	52		22(42)	60.7 +/- 9.2	NR	NR	NR	
Ludwig, 2011[37]	Chronic renal impairment	Total		100	48 Hours	NR	NR	NR	NR	NR	
		1	Control	51		9(19)	68	NR	NR	NR	
		2	MESNA	49		15(29)	68	NR	NR	NR	
Maioli, 2008[38]	Patients with chronic kidney dysfunction undergoing planned coronary angiography or intervention	Total		502	10 Days	NR	NR	NR	NR	NR	
		2	IV Isotonic Saline plus oral NAC	252		99 (39)	Median, 74 ; Range, 70-79	NR	NR	NR	
		3	IV Sodium Bicarbonate plus oral NAC	250		107 (43)	Median, 74 ; Range, 67-79	NR	NR	NR	
Maioli, 2011[39]	STEMI, ST-segment elevation-mycordial infarction	Total		0	3 Days	NR	NR	NR	NR	NR	
		1	No hydration	150		40(26.6)	64	NR	NR	NR	
		2	Late 0.9% saline	150		41(27.3)	66	NR	NR	NR	
		3	Early sodium bicarbonate	150		35(23.3)	65	NR	NR	NR	
Marenzi, 2006[40]	Acute MI, ST segment elevation acute MI	Total		354	NR	NR	NR	NR	NR	NR	
		1	placebo	119		22(18)	62.5	NR	NR	Current: 60(50)	
		2	Standard dose NAC	115		28(24)	62.5	NR	NR	Current: 57(50)	
		3	High dose NAC	118		18(15)	62.2	NR	NR	Current: 77(65)	

Evidence Table A. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Marenzi, 2012[41]	CKD-eGFR <60 ml/min/1.73 m 2 ,General	Total		170	72 Hours	NR	NR	NR	NR	NR	
		1	Saline Hydration	83		18(22)	73+/-7	NR	NR	Current: 7(13)	
		2	Furosemide plus matched hydration	87		19(22)	73+/-7	NR	NR	Current: 4(7)	
Marron, 2007[42]		Total		NR	48 Hours		NR	NR	NR	NR	
		1	Isotonic 0.9% saline	36		10	64	NR	NR	NR	
		2	Hypotonic 0.45% saline	35		13	68	NR	NR	NR	
Mueller, 2002[43]	General	Total		1383	30 Days	NR	NR	NR	NR	NR	
		1	Isotonic Saline hydration	685		178(26)	64	NR	NR	NR	
		2	.45% sodium chloride plus 5% glucose	698		176(25)	64	NR	NR	NR	
Ng, 2006[44]	Stable renal disease Cr >1.2	Total		95	72 Hours	(24.8)	68+/-10	NR	NR	NR	
		2	NAC	48		(18.8)	67+/-10	NR	NR	NR	
		3	Fenoldopam	47		(29.8)	69+/-11	NR	NR	NR	
Oguzhan, 2013[45]	Coronary angiography with serum creatinine <2.1 mg/dl	Total		90	NR	NR	NR	NR	NR	NR	
		2	AVH (amlodipine valsartan hydration group)	45		(40)	66.38	NR	NR	Ever: (48.9)	
		3	H (hydration group)	45		(33.3)	62.07	NR	NR	Ever: (53.3)	
Ozhan, 2010[46]	General	Total		130	48 Hours	53	54 +/-10	NR	NR	NR	
		2	NAC	70		30	55+/-8	NR	NR	NR	
		3	NAC + Atorvastatin	60		23	54+/-10	NR	NR	NR	
Pakfetrat, 2009[47]	General	Total		286	48 Hours	111(39)	57.9	NR	NR	NR	
		1	sodium chloride	96		34 (35)	58.5	NR	NR	NR	
		2	sodium bicarbonate in dextrose solution	96		40 (42)	57.8	NR	NR	NR	

Evidence Table A. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Pakfetrat, 2009[47] (continued)		3	sodium chloride plus oral Acetazolamide	94		47 (50)	57.5	NR	NR	NR	
Ratcliffe, 2009[48]	Renal insufficients, Cr Men >132.6 mg/dL Women >114.9 mg/dL and/or diabetics	Total		78	7 Days	32(40)	66	White: (13) Black: (33) Latino: (36) Asian/Pac: (19)	NR	NR	
		1	IV normal saline	15		6(40)	64	White: (20) Black: (27) Latino: (33) Asian/Pac: (20)	NR	NR	
		2	IV normal saline + IV/oral NAC	21		10(48)	65	White: (10) Black: (33) Latino: (33) Asian/Pac: (24)	NR	NR	
		3	IV NaHCO3	19		8(42)	67	White: (6) Black: (44) Latino: (33) Asian/Pac: (17)	NR	NR	
		4	IV NaHCO3+ IV/oral NAC	23		7(30)	65	White: (14) Black: (29) Latino: (43) Asian/Pac: (14)	NR	NR	
Recio-Mayoral, 2007[49]	Acute coronary Syndrome, acute coronary syndrome (ACS) patients who were admitted coronary care unit	Total		111	7 Days	NR	NR	NR	NR	NR	
		1	Saline + NAC after procedure	56		16(29)	64	NR	NR	NR	
		2	IV Bolus+ NAC before procedure +NAC after procedure	55		18(32)	65	NR	NR	NR	
Reinecke, 2007[50]	General	Total		424	Median 553 Days	NR	NR	NR	NR	NR	
		1	Hydration only	140		24(17.1)	67.9	NR	NR	Ever: 80(57.1)	

Evidence Table A. Participant Characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Reinecke, 2007[50] (continued)		2	Hydration + Dialysis	138		24(17.4)	67.9	NR	NR	Ever: 74(53.6)	
		3	Hydration + NAC	146		25(17.1)	66.7	NR	NR	Ever: 75(51.4)	
Rosenstock, 2008[51]	Chronic kidney disease (CKD) stages 3–4 (glomerular filtration rate 15–60 ml/min/1.73 m2	Total		283	72 Hours	NR	NR	NR	NR	NR	
		1	Naive to angiotensin blockade	63		23(37)	71.8	NR	NR	Current: 15(24)	
		2	Continue angiotensin blockade during and after procedure	113		52(46)	71.8	NR	NR	Current: 25(22)	
		3	Discontinue angiotensine blockade morning of procedure and 24hrs after procedure	107		41(38)	71.8	NR	NR	Current: 24(22)	
Schmidt, 2007[52]	General	Total		96	NR	NR	NR	NR	NR	NR	
		2	NAC plus sodium bicarbonate	47		14 (42)	67	NR	NR	NR	
		3	NAC plus standard hydration	49		11 (29)	68.3	NR	NR	NR	
Solomon, 1994[53]	Cr >1.6mg/dl - CrCl <60	Total		78	24 Hours	NR	NR	NR	NR	NR	
		1	Saline	28		5	67 +/- 11	NR	NR	NR	
		2	Mannitol + Saline	25		6	60 +/- 13	NR	NR	NR	
		3	Furosemide + Saline	25		13	63 +/- 13	NR	NR	NR	
Stevens, 1999[54]	Baseline serum creatinine greater than 1.8 mg/dl	Total		98	48 Hours	NR	NR	NR	NR	NR	
		1	IVF alone	55		21	69.6	NR	NR	NR	
		2	IVF + Furosemide + Dopamine + Mannitol	22		5	72.3	NR	NR	NR	
		3	IVF + Furosemide + Dopamine	21		6	67.0	NR	NR	NR	

Evidence Table A. ParticipantCharacteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Tamura, 2009	General	Total		144	7 days	NR	NR	NR	NR	NR	
		1	Normal saline	72		12(16.7_)	NR	NR	NR	NR	
		2	Normal Saline + NaHCO3	72		5.98(.83)	NR	NR	NR	NR	
Talati, 2012[55]	Coronary procedures	Total		104	72 Hours	NR	NR	NR	NR	NR	
		1	No Fenoldapam	52		17(33)	69.4	NR	NR	NR	
		2	Fenoldopam	52		13(25)	69.4	NR	NR	NR	
Trivedi, 2003[56]	General	Total		53	48 hours	NR	NR	NR	NR	NR	
		1	Oral hydration	26		0(0)	67.2 +/- 11.2	NR	NR	NR	
		2	IV Hydration (0.9% saline)	27		1(3.8)	68.5 +/- 8	NR	NR	NR	
Weisberg, 1994[57]	Stable plasma creatinine concentration greater or equal to 1.8 mg/dL	Total		26	:	NR	NR	NR	NR	NR	
		1	Saline	8		NR	NR	NR	NR	NR	
		2	Dopamine	8		NR	NR	NR	NR	NR	
Weisberg, 1994[57] (continued)		3	ANP	4		NR	NR	NR	NR	NR	
		4	Mannitol	6		NR	NR	NR	NR	NR	
Xinwei, 2009[58]	Acute Coronary syndrome: ACS was defined as any one of the following: (1) unstable angina pectoris; (2) ST-segment elevation myocardial infarction; and (3) non–ST-segment elevation myocardial infarction	Total		228	48 Hours	NR	NR	NR	NR	NR	
		2	Simvastatin 20	115		67 (58)	NR	NR	NR	NR	
		3	Simvastatin 80	113		79 (70)	NR	NR	NR	NR	

Evidence Table A. ParticipantCharacteristics for studies comparing interventions to prevent development of CIN (continued).

Author, year	Study Population	Arm*	ARM define	N	Follow-up Period	Sex, N female (%)	Age, mean unless otherwise specified	Race	Education	Smoking status	Comments
Yin, 2013[59]	Coronary Care Unit, acute STEMI and acute (NSTEMI) requiring urgent coronary intervention due to ongoing ischemic symptoms	Total		204	3 Days	NR	NR	NR	NR	NR	
		1	No probucol	108		34(31.5)	Median: 12.5;Range: 65.1	NR	NR	NR	
		2	Probucol	96		29(30.2)	65.1;Range: 10.5	NR	NR	NR	

ACS=Acute Coronary Syndrome, AVH= amlodipine valsartan hydration group, CCS=Canadian Cardiovascular Society, CHF=Chronic Heart Failure, CIN=Contrast Induced Nephropathy, CKD=Chronic Kidney Disease, CK-MB=Creatine Kinase MB, CPK=Creatine Phosphokinase, Cr=Creatinine, CrCl=Creatinine Clearance, CRF=Chronic Renal Failure, eGFR=Estimated Glomerular Filtration Rate, GFR=Glomerular Filtration Rate, H=hydration group, HD=Hemodialysis, ICU=Intensive Care Unit, IU=International Units, IV=Intravenous, IVF=Intravenous Fluid, Mg/dl=milligram per deciliter, Mg/kg/hour=Milligram per kilogram per hour, Mg/kg=milligram per kilogram, MI=Myocardial Infarction, ml/min/1.73m^2=milliliter per minute per 1.73 meter squared, Ml/min=milliliter per minute, Mmol/l=millimole per liter, N=Sample Size, NAC=N-acetylcysteine, NR=Not Reported, NSTEMI=non-ST-segment elevation-mycordial infarction, OHT=Orthotopic Heart Transplantation, PCI=Percutaneous Coronary Intervention, SCr=Serum Creatinine, SD=Standard Deviation, SrCr=Serum Creatinine, STEMI= ST-segment elevation-mycordial infarction, UA=Unstalbe Angina, Ug/kg/min=microgram per kilogram per minute, Umol/l=micromole per liter

* if there is no “Arm 1” there is no control group.

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Abizaid, 1999[1]	2	RCT/ Controlled	No	NR	NR	Single-center	Serum creatinine ≥1.5 mg/dl. No preexisting ARF, not on chronic dialysis, No electrocardiographic or enzymatic evidence of acute myocardial infarction, left ventricular ejection fraction >20%, No allergy to contrast medium, and No pregnancy.	
Acikel, 2010[2]	2	RCT/ Controlled trial	No	NR	Inpatient (including ICU)	Single-center	coronary angiography; GRF > 60 ml/min; a low-density lipoprotein (LDL) level of more than 70 mg/dl and receiving no cholesterol-lowering medication	
Adolph, 2008[3]	2	RCT/ Controlled	No	NR	NR	Single-center	>18 years, serum creatinine > 106umol/l (1.2 mg/dl) and/or eGFR of 63 ml/min/1.73 m2, No Acute myocardial infarction requiring primary or rescue coronary intervention, allergies to trial medication, exposure to contrast medium within the preceding 7 days, thyroid dysfunction, pregnancy, uncontrolled hypertension (systolic blood pressure >180mmHg or diastolic blood pressure >100mmHg), life-limiting concomitant disease, pulmonary edema, chronic dialysis, and administration of dopamine, manitol, fenoldopam, or N-acetylcysteine..	
Allaqaband, 2002[5]	2	RCT/ Controlled	No	NR	Inpatient (including ICU)	NR	scheduled to undergo cardiovascular intervention with radio contrast agent; creatinine of more than 1.6 mg/dl or an estimated creatinine clearance of less than 60 ml/min	
Aslanger, 2012[6]	2	RCT/ Controlled	No	2007 to 2009	NR	Single-center	>30years, Primary angioplasty,; Other Risk factors, ST-segment elevation myocardial infarction, angioplasty within 12 hours of symptoms No allergies to NAC Not on dialysis	
Bader,2004[7]	2	RCT/ Controlled	No	NR	NR	NR	Computer tomography (CT) or digital subtraction angiography (DSA); no Pregnancy , no uncontrolled arterial hypertension, no severe heart failure (NYHA II – IV), no liver failure and no nephrotic syndrome. Serum creatinine levels 0.6-1.2 mg/dl. Stable serum creatinine concentrations only were included	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Baskurt, 2009[8]	2	RCT/ Controlled	No	2008 to 2010	NR	Multi-center	>70year, coronary or peripheral arterial diagnostic intra- vascular angiography or percutaneous intervention chronic renal failure (stable serum creatinine concentrations >132.6 umol/L, at least 1 risk factor for contrast-induced acute kidney injury: age > 70 years, chronic renal failure (stable serum creatinine concentrations > 132.6 mol/L [1.5 mg/dL]), diabetes mellitus, clinical evidence of congestive heart failure, left ventricular ejection fraction < 0.45, or hypotension. no patient on dialysis and those with ST-segment elevation myocardial infarction undergoing primary angioplasty, no woman pregnant, breastfeeding, or aged 45years and not using contraceptive methods	
Briguori, 2004[10]	2	RCT/ Controlled	No	2009 to 2010	NR	NR	>19years, coronary angiography and/or percutaneous coronary intervention; Impaired renal function; creatinine clearance (CrCl) <60 ml/min, no pregnancy, no lactation, not received contrast media <7 days before the procedure, no emergent CAG in which sufficient pre-procedural hydration was unavailable, no acute renal failure, no end-stage renal disease requiring dialysis, no history of hypersensitivity reaction to contrast media, no cardiogenic shock, no pulmonary edema, and no mechanical ventilator support	
Briguori, 2004[9]	2	RCT/ Controlled	No	2003 to 2003	NR	Single-center	Scheduled for coronary or peripheral angiography/angioplasty,; serum creatinine >1.5mg/dl and/or creatinine clearance <60ml/min,,,,	
Brigouri, 2007[11]	2	RCT/ Controlled	No	2005 to 2006	NR	NR	>18 years, stable serum creatinine concentration >2.0mg/dl and/or eGFR <40ml/min/1.73m^2. No serum creatinine ?8mg/dl, history of dialysis, multiple myeloma, pulmonary edema, ami, recent exposure to contrast (2 days of study), pregnancy, or had administration of theophylline, dopamine, mannitol or fenoldopam.	
Briguori, 2011[12]	2	RCT/ Controlled	Yes	2009 to 2010	NR	Multi-center	Scheduled for coronary/peripheral angiography or angioplasty, estimated glomerular filtration rate (eGFR), with chronic kidney disease, No presence of: AMI, acute pulmonary edema, cardiogenic shock, dialysis, multiple myeloma, sodium bicarbonate, theophyline, dopamine, mannitol or fenoldopam 48 hours before procedure, no recent administration of iodinated contrast media, no current enrollment in any other study.	
Mueller, 2002[43]	2	RCT/ Controlled	No	1998 to 1999	NR	NR	Elective or emergency angioplasty; no end-stage renal failure with regular hemodialysis, no cardiogenic shock, and no mechanical ventilation,	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Chen, 2008[13]	2	RCT/ Controlled	No	2004 to 2006	Inpatient (including ICU)	Multi-center	Percutaneous coronary intervention, the coronary anatomy suitable for PCI, no emergency coronary artery bypass grafting (CABG) being required, no patients in chronic peritoneal or hemodialysis treatment, no acute myocardial infarction (AMI) at admission. Myocardial ischemia.	
Cho, 2010[14]	2	RCT/ Controlled	No	NR	Inpatient (including ICU)	Single-center	>18years, CAG,; SCr >=1.1mg/dl, no serum creatinine levels greater than 8.0 mg/dL, no change in serum creatinine levels of at least 0.5 mg/dL during the previous 24 hours, no preexisting dialysis, no multiple myeloma or other myeloproliferative disease, no current decompensated heart failure or significant change in base- line New York Heart Association Class, no current myocardial infarction, no symptomatic hypokalemia, uncontrolled hypertension (treated systolic blood pressure > 200 mmHg or diastolic blood pressure > 100 mmHg), no exposure to radio contrast within 7 days of enrollment into this study, no emergency catheterization, no allergy to radiographic contrast, no pregnancy, administration of dopamine, no mannitol, fenoldapam, or NAC during the time of the study, no exacerbation of chronic obstructive pulmonary disease, no serum bicarbonate greater than 28 mEq/L, and sodium less than 133 mEq/L	
Demir, 2008[15]	1	RCT/ Controlled	No	NR	Inpatient (including ICU)	Single-center	CT, No diabetes, no chronic renal failure, no uncontrolled hypertension or hypotension, no pregnancy, no ESRD, no renal transplantation, no dialysis history, no sensitivity to CM, no nephrotoxic drug use (NSAIDs, aminoglycoside, etc)	
Durham, 2002[60]	2	RCT/ Controlled	No	NR	NR	Multi-center	>18years, coronary angiography and/or PCI, mild to moderate renal dysfunction with serum creatinine (SCr) ≥ 1.1 mg/dL or creatinine clearance ≤ 60 mL/min, Does not have contrast-agent hypersensitivity, pregnancy-lactation, decompensated heart failure, pulmonary edema, emergency catheterization, acute renal failure or end-stage renal failure	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Erol, 2013[16]	2	RCT/ Controlled	No	2004 to 2006	NR	Single-center	Undergoing cardiac catheterization; serum creatinine >1.1mg/dl, no acute myocardial infarction requiring primary/rescue coronary intervention within 24 hours. No cardiogenic shock, acute renal failure, peritoneal dialysis/hemodialysis, planned post contrast dialysis, or history of intravascular administration of contrast agents or anticipated re-administration of contrast agents within the following 4-days.	
Firouzi, 2012[17]	2	RCT/ Controlled	No	NR	NR	Single-center	Undergoing primary PCI, CVD; acute myocardial infarction; Patients with AMI undergoing primary PCI were eligible if their symptoms lasted 12 h and if they had ST-segment elevation of 0.1 mV in 2 extremity leads or 0.2 mV in 2 pre-cordial leads. No previous fibrinolysis in < 12 hours, known N-acetylcysteine allergy, chronic dialysis, and pregnancy. No contraindications to magnetic resonance imaging (MRI)	
Frank, 2003[18]	2	RCT/ Controlled trial	No	2000 to 2001	Inpatient (including ICU)	Single-center	>18; coronary angiography; not requiring HD; ,; ; Stable SrCr (> 3mg/dl); no allergy to contrast medium; not pregnant; no acute renal failure	
Gu, 2013[19]	2	RCT/ Controlled	No	2009 to 2011	Inpatient (including ICU)	Single-center	coronary angiography or percutaneous coronary intervention; New York Heart Association stage < 4; no other serious illness that is inappropriate for hydration.	
Gunebakmaz, 2012[20]	2	RCT/ Controlled trial	No	2008 to 2009	NR	Single-center	coronary angiography or ventriculography; , excluded Baseline Creatinine > 1.2 mg/dl	
Hafiz, 2012[21]	2	RCT/ Controlled	No	2004 to 2006	NR	Multi-center	>18, undergoing coronary and peripheral angiogram, serum creatinine >1.6 mg/dl in non-diabetics and >1.4 mg/dl in diabetics or an estimated glomerular filtration rate (eGFR) of <50 ml/min/1.73 m^2 Not on dialysis. Stable renal function (defined as no change in serum creatinine of >0.4 mg/dl within 48 hours prior to the index procedure. No pulmonary edema, no serum bicarbonate level >34 mmol/L. Have not received fenoldopam, mannitol, dopamine, or NAC within 48 hr prior to the index procedure. Was not in cardiogenic shock. No allergies to contrast media, not pregnant, and able to provide informed consent	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Hans, 1998[22]	2	RCT/ Controlled	No	1989 to 1994	NR	NR	Arteriography of the abdominal and lower extremity arteries by catheter techniques; Serum creatinine greater than or equal to 1.4mg/dl, Other Risk factors, peripheral arterial occlusive disease (see #16 for explanation), Patients not taking aminoglycosides or not undergoing combined studies (such as carotid and lower extremity arteriograms) [The Methods section mentions that all patients had disabling claudication or lower extremity ischemia, but those were not specified as inclusion criteria per se. This would probably be more a result than something in the Methods section, but because it is listed there, it will be added here. It is most likely something that is a finding based on the patient population that would undergo the imaging that was used. The text also mentions that they selected patients who underwent the imaging test described because of peripheral arterial occlusive disease, so the latter is being added as an inclusion criterion]	
Hashemi, 2005[23]	2	RCT/ Controlled	No	2004 to 2004	NR	Single-center	Undergoing coronary angiography, Contrast used for each patient 100-300mls. No calcium antagonists, ACE-I, or theophylline prescribed within 2 days before procedure. Baseline creatinine below 2 mg/dl	
Heguilen, 2013[24]	1,2	RCT/ Controlled	No	NR	NR	Single-center	> 18years, scheduled for cardiac catheterization or arteriographic procedure, Stable serum creatinine >1.25 mg/dL or Cockcroft-Gault-estimated creainine clearance <45 ml/min non-emergency catheterization; without pulmonary edema; no preexisting dialysis; non recent exposure to CM; no history of multiple myeloma; controlled hypertensives; without hemodynamic instability; not being treated with the following medications: dopamine, mannitol, fenoldopam, aminophylline, theophylline ascorbic acid or NAC; Non pregnant or childbearing women; or not hypersensitive to CM or NAC. The SCr shouldn't be [4.5 mg/dl ([364.5 lmol/l) or no change in SCr of at least 0.5 mg/dl (44.2 lmol/l) within the previous week.	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Holscher, 2008[25]	2	RCT/ Controlled	No	NR	NR	Single-center	>14years and <79years, coronary angio-PCA- CT scan- IV pyelography; No acute renal failure, maintenance dialysis, history of acute myocardial infarction, left ventricular ejection fraction (EF) ≤ 25%, allergy to contrast media, pregnancy, contraindications for theophylline use such as untreated high-grade arrhythmia or history of seizure, or use of acetylcysteine.	excluded HD and ARF
Huber, 2006[26]	1,2	RCT/ Controlled	No	2006 to 2008	NR	Single-center	Elective coronary Angiography; no hemodialysis creatinine clearance <60ml/min, No treatment with a statin, contraindication to statin treatment, previous contrast media administration (within 10 days of study entry), end-stage renal failure requiring dialysis, or informed refusal of consent	
Kimmel, 2008[27]	2	RCT/ Controlled	No	2005 to 2006	NR	Single-center	>18years, coronary angiography with or without PCI, not on dialysis; no acute renal failure or ESRD, no participation in an investigational drug or device trial within 30 days; not having received CM within 7 days of study entry; not scheduled major surgical intervention; no history of hypersensitivity reaction to iodinated CM; unstable hemodynamic conditions; use of N-acetylcysteine (NAC), metformin, or non-steroidal anti-inflammatory drugs within 48 hour to the procedure; intravenous use of diuretics or mannitol; and pregnancy or lactation. CrCl <60ml/min	
Kinbara, 2010[28]	2	RCT/ Controlled trial	No	2006 to 2007	Inpatient (including ICU)	Single-center	Coronary angiography; Other Risk factors,Stable coronary artery disease; Exclusion criteria of this study included acute myocardial infarction requiring primary or rescue PCI, use of vasopressors before PCI, cardiogenic shock, current peritoneal dialysis or hemodialysis, planned post-contrast dialysis, or allergies to the medications being studied	
Klima, 2012[29]	1,2	RCT/ Controlled	No	2005 to 2009	NR	Multi-center	>18years, undergoing IA or IV radiocontrast procedure within 24 hours, 93 mmol/L for women and .117 mmol/L for men or estimated glomerular filtration rate (eGFR) ,60 mL/min/1.73 m2, No pre-existing dialysis, no allergies to radiographic contrast, not pregnant, no severe heart failure, no NAC 24 hours before contrast procedure, no clinical condition requiring continuous fluid therapy	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Koc, 2012[30]	2	RCT/ Controlled	Yes	NR	NR	NR	Patients who were ≥18 years of age, with a creatinine clearance (CrCl)≤60mL/min and/or baseline serum creatinine level (SCr)≥1.1 mg/dL. No contrast-agent hypersensitivity, pregnancy-lactation, decompensated heart failure, pulmonary edema, emergency catheterization, acute renal failure and end-stage renal failure..	
Kong, 2012[31]	2	RCT/ Controlled	No	2010 to 2010	NR	NR	Coronary angiography or PCI; no renal dysfunction, No definitive or suspected coronary artery disease, no MI, baseline serum creatinine below 110 umol/L, no LV dysfunction with LVEF <45%,no blood electrolyte disturbances or liver dysfunction, 18-80 years age	
Kotlyar, 2005[32]	2	RCT/ Controlled	No	NR	NR	Single-center	Elective coronary angiography and/or coronary intervention; no acute coronary syndrome requiring emergent coronary angiography or primary coronary inter- vention, no cardiogenic shock, no iodinated contrast media administration within a month or N -acetylcysteine within 48 h before the study entry, no current dialysis or a serum creatinine concentration N 1.4 mg/dL for men, or N 1.2 mg/ dL for women, no thyroid diseases, or no allergy to the study medication. Normal renal function (serum creatinine <1.4 mg/dl in men and <1.2 mg/dl in women)	
Krasuski, 2003[33]	2	RCT/ Controlled	Yes	NR	Inpatient (including ICU) Outpatient	Single-center	Elective cardiac catheterization; moderate renal insufficiency-Serum creatinine from 1.6mg/dl to 3mg/dl, Not requiring emergent or urgent procedures, not admitted for planned catheter based intervention, no absolute contra indication to or absolute indication for iv hydration, not on ACE inhibitor within 72h of procedure, not received iodinated contrast, aminoglycoside or nephrotoxic agent within 96h of procedure.	
Yin, 2009[35]	2	RCT/ Controlled	No	2007 to 2008	Inpatient (including ICU)	Single-center	Coronary angiography and/or PCI,CVD; NYHA 1-3 (<4); CR <3	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Lawlor, 2007[34]	2	RCT/ Controlled	No	NR	Outpatient	Single-center	angiography for peripheral vascular disease and aneursymal disease; stable chronic renal impairment, Patients with serum creatinine concentrations greater than 140 mmol/L or estimated creatinine clearance < 50 mL/min were eligible, patients with stable, chronic renal insufficiency patients with hemodynamic stability, those who no medical reasons to not tolerate the hydration protocol, No known sensitivity to NAC (gastrointestinal intolerance, urticaria), and those able to provide informed consent	
Lehnert, 1998[61]	1,2	RCT/ Controlled	No	NR	NR	Single-center	Angiography with at least 1.2 ml/kg/BW contrast medium dose (specific type of test was not listed as inclusion criterion); All patients with stable serum creatinine of at least 1.4mg/dl undergoing angiography with contrast medium dose of greater than or equal to 1.2ml/kg BW, non-pregnant women, no known allergy to contrast medium, no prior exposure to contrast medium in past 14 days before the start of the protocol, and no diagnosis of end-stage renal disease	
Li, 2011[36]	2	RCT/ Controlled	No	NR	Inpatient (including ICU)	Single-center	Elective coronary angiography, no changes in PCr ≥ 0.5 mg/dL in the 24 hours prior to the test, no advanced renal failure, or dialysis (stage 4 and 5 of the National Kidney Foundation classification 28), no pregnancy, no contrast allergy, no severe clinical heart disease, and/or ejection fraction (EF) <30%, no acute myocardial infarction in the previous 2 weeks or hemodynamic instability necessitating inotropic support, no uncontrolled hypertension, no liver disease, no chronic obstructive pulmonary disease, N-acetylcysteine or need for intercurrent serum therapy, and no significant concomitant disease, such as malignant tumors, uncontrolled diabetes mellitus, hypothyroidism, or hyperthyroidism	
Ludwig, 2011[37]	1,2	RCT/ Controlled	No	2002 to 2004	NR	Single-center	Cardiac catheterization- angio-CT; 1.7mg/dl, NO patients already undergoing dialysis, no patients who had acute renal failure, or patients who had received iodinated contrast media within 7 days prior to the study. no patients with a known allergy to MESNA, no pregnant women, and no patients receiving dopamine, mannitol, or NAC	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Maioli, 2008[38]	2	RCT/ Controlled trial	No	2005 to 2006	Inpatient (including ICU)NR	Single-center	Coronary angiography; Chronic Kidney Dysfunction; No creatinine clearance ≥ 60 ml/min, no administration of contrast medium within the previous 10 days, no end stage renal disease	
Maioli, 2011[39]	2	RCT/ Controlled	Yes	2004 to 2008	NR	Single-center	Candidate for primary PCI with STEMI, No end stage renal failure requiring dialysis, No contrast media given within the previous 10 days.	
Marenzi, 2012[41]	2	RCT/ Controlled	No	2008 to 2011	Inpatient (including ICU)	Single-center	>18years and <85yearsv, coronary angiography and, when indicated, percutaneous coronary intervention (PCI), CKD-eGFR < 60 ml/min/1.73 m^2 no primary or rescue PCI and angiography procedures requiring a direct renal injection of contrast, no cardiogenic shock, no overt congestive heart failure, no acute respiratory insufficiency, no recent acute kidney injury, no chronic peritoneal or hemodialysis treatment, no known furosemide hypersensitivity, no receipt of intravenous contrast within 10 days before the procedure or another planned contrast-enhanced procedure in the following 72 h, and no contraindications to placement of a Foley catheter in the bladder.	
Marron, 2007[42]	2	RCT/ Controlled	No	NR	Emergency department	Single-center	Emergency contrast-enhanced CT; Renal insufficiency-serum creatinine concentration greater than 106 µmol/L (1.2 mg/dL), no pregnancy, no end-stage renal failure necessitating dialysis, no suspicion of acute renal obstruction (complicated renal colic), no asthma, no severe cardiac failure or hemodynamically unstable condition contraindicating IV hydration, and no non-urgent indications for CT.	
Ng, 2006[44]	2	RCT/ Controlled	Yes	NR	Inpatient (including ICU) Outpatient	Single-center	Cardiac catheterization, Cr>1.2,	
Oguzhan, 2013[45]	2	RCT/ Controlled trial	No	2010 to 2011	Inpatient (including ICU)	Single-center	Serum creatinine concentration of < 2.1 mg/dL. No acute STEMI, manifest congestive heart failure, hemodynamic instability, prior exposure to contrast media within 7 days, or use of a nephrotoxic drug within 48 h and contraindication for amlodipine and valsartan prescription	
Ozhan, 2010[46]	2	RCT/ Controlled	No	NR	NR	Single-center	Coronary or peripheral angiography and or PCI; CR > 1.5, creatinine clearance <60ml/min	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Pakfetrat, 2009[47]	2	RCT/ Controlled trial	No	2007 to 2008	Inpatient (including ICU)	Single-center	Coronary angiography or percutaneous coronary intervention; No recent (two days) exposure to contrast media, hypotension, intra-aortic balloon pump, pulmonary edema, dialysis, electrolyte and acid base disturbances, known sensitivity to AZ,not receiving therapies affecting renal function, for example mannitol, dopamine, and theophylline, or unwilling to give written informed consent	
Ratcliffe, 2009[48]	2	RCT/ Controlled	No	2007 to 2008	Inpatient (including ICU) Outpatient	Single-center	coronary angiography or coronary angioplasty; elevated serum creatinine (greater than 132.6 µmol/L in men, and greater than 114.9 µmol/L in women) or reduced calculated creatinine clearance (less than 1.002 mL/s) using the Cockcroft-Gault formula, DM on oral antiglycemic or insulin therapy, no acute MI, no Signs of heart failure or EF <35%, no cardiogenic shock, no hypertrophic or restriction cardiomyopathy, no contrast media exposure in last week, no previous reaction to contrast media, no renal transplatation, no dialysis, no severe comorbid illness, no use of dopamine, mannitol, or fenoldopam, no newly diagnosed uncontrolled DM, no inability to follow-up	
Recio-Mayoral, 2007[49]	2	RCT/ Controlled	No	2004 to 2005	Inpatient (including ICU)	Single-center	PCI; Other Risk factors, MI, Patients with MI treated with primary PCI or rescue PCI, as well as patients with high-risk non–ST-segment elevation ACS needing urgent revascularization, were included. NO patient with end-stage renal failure on dialysis, uncontrolled hypertension (systolic blood pressure 160 mm Hg and/or diastolic blood pressure 100 mm Hg) and signs of cardiac failure not responding to medical treatment, No known severe aortic valve stenosis (area 1.0 cm2), No allergy to iodated contrast or NAC, and not pregnancy	
Reinecke, 2007[50]	2	RCT/ Controlled	No	2001 to 2004	Inpatient (including ICU)	Single-center	Elective coronary angigraphy; Serum creatinine concentrations ≥1.3 mg/dl and ≤3.5 mg/dl. Absence of acute or recent (within 30 days) myocardial infarction, congestive heart failure (New York Heart Association class IV), recipient of transplanted organs, monoclonal gammopathy, and/or previous contrast medium administration within 7 days	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Rosenstock, 2008[51]	2	RCT/ Controlled	No	NR	NR	Single-center	Coronary angiography, chronic kidney disease (CKD) stages 3–4 (glomerular filtration rate 15–60 ml/min/1.73 m^2, no acute ST elevation myocardial infarction within 2 weeks, no New York Heart Association functional class IV heart failure, no acute renal failure preceding angiography (defined as an increase in serum creatinine of [0.5 mg/dl from baseline values), no hyperkalemia (K[5.0 meq/l), GFR B15 ml/min/1.73 m^2 as calculated by the abbreviated MDRD formula, no prior cardiac catheterization within one month, no hemodynamic instability (defined as SBP\90 on at least two consecutive readings or patients requiring pressors), no poorly controlled hypertension (systolic blood pressure [180 mmHg on at least two consecutive readings), no patients taking combination ACEI/ARB therapy. no patients that had taken the ACEI or ARB less than 24 h before enrollment and randomization	
Schmidt, 2007[52]	2	Des_Pro	No	2002 to 2005	Inpatient (including ICU)	Single-center	coronary angiography; to have received at least one 600mg oral dose of NAC before the procedure, no carotid or vascular angiographies performed instead of coronary angiography, no NAC administered before angiography	
Shemirani, 2012[62]	2	RCT/ Controlled	No	2006 to 2007	Inpatient (including ICU)	Single-center	Percutaneous coronary intervention; included patients with serum Cr < 1.5 mg/dL or glomerular filtration rate > 60 mL/min, no consumption of both captopril and furosemide, no PCI during acute myocardial infarction, heart failure of class III–IV New York Heart Association (NYHA), no previous exposure to contrast media in the 14 days before randomization, no need for emergency coronary artery bypass graft (CABG) during PCI.	
Solomon, 1994[53]	2	RCT/ Controlled trial	No	NR	NR	Single-center	cardiac angiography; Cr>1.8	

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Stevens, 1999[54]	2	RCT/ Controlled trial	Yes	NR	NR	Single-center	Elective coronary angiography; baseline SrCr > 1.8 mg/dl; Other Risk factors, No acute myocardial infarction requiring primary or rescue coronary intervention, no use of vasopressors prior to the procedure, no cardiogenic shock, no current peritoneal or hemodialysis, no planned postcontrast dialysis, no allergies to the study medications; Exclusion criteria included acute myocardial infarction requiring primary or rescue coronary intervention, use of vasopressors prior to the procedure, cardiogenic shock, current peritoneal or hemodialysis, planned postcontrast dialysis, or allergies to the study medications	
Talati, 2012[55]	1,2	Des_Pro	No	NR	NR	Single-center	underwent catheter based coronary procedure	
Tamura, 2009	2	RCT	No	NR	Inpatient	Multi-center	>20 years and serum creatinine (Cr) level 1.1 to 2.0 mg/dl, No allergy to contrast medium, no pregnancy, no history of dialysis, no exposure to contrast medium within the preceding 48 hours of the study, acute coronary syndrome within the preceding 1 month of the study, no severe symptoms of heart failure (New York Heart Association functional class IV),no left ventricular ejection fraction _25%, severe chronic respiratory disease, no single functioning kidney, and no administration of *N*-acetylcysteine, theophylline, dopamine, or mannitol.	
Trivedi, 2003[56]	2	RCT/ Controlled	No	NR	Inpatient (including ICU).	Single-center	Non-emergency coronary angiography calculated creatinine clearance greater than 20 ml/min, Absence of clinically decompensated heart failure and states of decreased effective arterial volume (such as nephrotic syndrome, cirrhosis of liver). Willingness of the participant to participate. Approval by the patient's primary treating team.	Some patients were known to be in the hospital at baseline; the paper does not specify if some patients were recruited from an outpt setting as well

Evidence Table B. Study characteristics for studies comparing interventions to prevent development of CIN (continued).

Author, Year	Key Question	Design	Sub group analysis	Recruitment date	Recruitment setting	Multi or single center	Inclusion criteria	Comments
Weisberg, 1994[57]	2	RCT/ Controlled	No	NR	NR	Single-center	elective cardiac cath; Cr >= 1.8 mg/dL, Absence of the following: NYHA Class IV congestive heart failure, evidence of liver dysfunction, hemodynamic instability, allergy to contrast medium, prior exposure to contrast medium within seven days of the experimental protocol, pregnancy.	
Xinwei, 2009[58]	2	RCT/ Controlled trial	No	2007 to 2008	Inpatient (including ICU)	Single-center	Percutaneous Coronary Intervention; Other Risk factors,Acute Coronry Syndrome: ACS was defined as any one of the following: (1) unstable angina pectoris; (2) ST-segment elevation myocardial infarction; and (3) non–ST-segment elevation myocardial infarction; ; The following exclusion criteria were used: pregnancy, lactation, previous contrast media exposure within 7 days of study entry, acute renal failure, end-stage renal disease requiring dialysis, alanine transaminase elevation, history of hypersensitivity to contrast media, multiple myeloma, cardiogenic shock, and left ventricular ejection fraction 40%. Also, patients who had used statins within 30 days were excluded. Patients who had undergone primary PCI or had undergone PCI within 5 days after enrollment were excluded from the present study	
Yin, 2013[59]	2	RCT/ Controlled	No	2009 to 2010	Inpatient (including ICU)	Single-center	primary or urgent coronary angioplasty; Other Risk factors, patients with acute ST elevation myocardial infarction (STEMI) requiring primary coronary intervention and acute non-ST elevation myocardial infarction (NSTEMI) requiring urgent coronary intervention, Patients presenting within 12hrs after onset of symptoms. No patients with cardiogenic shock Patients with Scr <3.0 mg/dl and patients not on long-term dialysis	

ACE= Angiotensin Converting Enzyme, ACEI=Angiotensin Converting Enzyme Inhibitor, ACS=Acute Coronary Syndrome, AMI=Acute Myocardial Infarction, ARB=Angiotensin Receptor Blocker, ARF=Acute Renal Failure, AZ=Acetazolamide, BW=Body Weight, CABG=Coronary Artery Bypass Grafting, CAG= Coronary angiogram, Cc/kg=cubic centimeter per kilogram, CE-MDCT=Contrast Enhanced Multi-detector Computer Tomography, CHF=Chronic Heart Failure, CIN=Contrast Induced Nephropathy, CKD=Chronic Kidney Disease, CM=Contrast Media, Cr=Creatinine, CrCl=Creatinine Clearance, CRF=Chronic Renal Failure, CT=Computer Tomography, CVD=Cardiovascular Disease, EF=Ejection Fraction, eGFR=estimated Glomerular Filtration Rate, ESRD=Endstage Renal Disease, GFR=Glomerular Filtration Rate, GI=Gastrointestinal, H=hour, HD=Hemodialysis, IA=Intrarterial, ICU=Intensive Care Unit, IV=Intravenous, LDL=Low Density Lipoprotein, LVEF=Left Ventricular Ejection Fraction, MDCT=Multi-detector Computer Tomography, MDRD= Modification of Diet in Renal Diseases, mEq/l=milliequivalents per liter, Mg/dl=milligrams per deciliter, mg=milligram, MI=Myocardial Infarction, Ml/min/1.73m^2=milliter per minute per 1.73 meter squared, Ml/min=milliliter per minute, mmHG=millimeter of Mercury, Mol/l=mole per liter, NAC=N-acetylcysteine, NR=Not Reported, NSAID=Non-steroid Inflammatory Drug, NYHA=New York Heart Association, PCI=Percutaneous Coronary Intervention, PCr=Plasma Creatinine, RCT=Randomized Controlled Trial, SrCr=Serum Creatinine, STEMI= ST Elevation Myocardial Infarction, T2DM=Type 2 Diabetes Mellitus, Umol/l=micromole/liter, Yrs=years

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN.

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Abizaid,1999[1]	Low osmolarity contrast medium (Hexabrix, Mallinkrodt, St. Louis, Missouri)	IA	Not specified, Define, mean 202 ml. Range75-450ml	1	0.45% IV Normal Saline(1 ml/kg/hour)	IV	1 ml/kg/hour 0.45% IV normal saline, Saline 12hrs before and 12hrs after, Prior to CM administration After CM admin	All patients received 0.45% normal saline (1 ml/kg/hr)
				2	Dopamine (2.5 ug/kg/min) plus 0.45% IV Normal Saline (1 ml/kg/hour)	IV	2.5 ug/kg/min dopamine + 0.45% IV normal saline hydration 1ml/kg/hour, Saline 12hrs before and 12hrs after-others not stated, Prior to CM administration After CM admin	
				3	Aminophylline (4 mg/kg followed by a drip of 0.4 mg/kg/hour) plus 0.45% IV Normal Saline (1 ml/kg/hour)	IV	4 mg/kg aminophylline followed by a drip of 0.4 mg/kg/hour+0.45% IV normal saline hydration 1ml/kg/hour, Saline 12hrs before and 12hrs after-others not stated, Prior to CM administration After CM admin	
Acikel, 2010[2]	Iohexol	IA	66-260ml. Comparable between groups	1	Control	NR		Saline 1ml/kg/h 4h prior until 24 after procedure
				2	Atorvastatin	Oral	40mg/d, 3 days, Prior and after CM administration	Saline 1ml/kg/h 4h prior until 24 after procedure
				3	Chronic statins	Oral	At least a month, Prior and after CM administration	Saline 1ml/kg/h 4h prior until 24 after procedure
Adolph, 2008[3]	Iodixanol	IA	Mean Arm 1 138 +/- 52 ml ml; Arm 2 141 +/- 50	1	Saline plus dextrose	IV	154 mEq/l of sodium chloride in 5% dextrose solution , 2 ml/kg of body weight per hour for 2 h before, at a rate of 1 ml/kg of body weight per hour during, and for 6 h after the administration of iodixanol.	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Adolph, 2008[3] (continued)				2	Sodium Bicarbonate in 5% dextrose	IV	154 mEq/l of sodium bicarbonate in 5% dextrose solution, 2 ml/kg of body weight per hour for 2 h before, at a rate of 1 ml/kg of body weight per hour during, and for 6 h after the administration of iodixanol.	
Alessandri, 2013 [4]	Iomeprol	IA	1.5ml-3ml/kg, Not specified	1	Sodium Chloride infusion	IV	Saline 0.9% 500mls thrice daily, 12hrs before and a day after, Prior to CM administration During CM administration After CM administration	
Alessandri, 2013 [4] (continued)				2	Sodium bicarbonate + NAC	Oral, IV	NAC 600mg bid + 160 meq of Na 2 HCO 3 in 350 ml of 5% glucose solution 2 ml/kg/h, NAC-day before to day after, nahco3-2hrs before to 6hrs after, Prior to CM administration During CM administration After CM administration	
Allaqaband, 2002 [5]	LOCM	IA	Mean: Arm1 1.47 ml/kg (SD 0.80), Arm2 1.52ml./kg (SD 0.81), Arm3 1.63ml/kg (SD 0.67), Not specified	1	0.45% saline	IV	0.45% Saline: 1 ml/kg/hr, 12 hour before procedure, during procedure, and 12 hours after procedure, Prior to CM administration During CM administration After CM administration	
				2	0.45% saline + nac	IV	Saline: 1 ml/kg/hr + NAC: 600mg 2x daily, Saline same as Arm 1, NAC: given 12 hours before and 12 hours after procedure, Prior to CM administration During CM administration After CM administration	
				3	0.45% saline + fenoldopam	IV	Saline: 1 ml/kg/hr + Fenoldopam: 0.1 microgram/kg/hr, Saline: same as Arm 1, Fenoldopam: starting 4 hours before procedure and ending 4 hours after., Prior to CM administration During CM administration After CM administration	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
				2	N-acetylcysteine	Oral	600mg b.i.d, 24hrs before and 24hrs after, Prior and After CM administration	
Aslanger, 2012 [6]	Ioxaglate	IA	Not specified, Define, Mean: Arm1 - 204ml, Arm2 - 193ml, Arm3 - 205ml	1	Placebo	IV	12ml saline during procedure, placebo capsules presumablyt twice daily for 2 days, 48 hours, During CM administration After CM administration	0.9% saline for 12 hours at 1 ml/kg/hr
				2	Iv nac	IV	1200mg IV during procedure, 1200mg by mouth twice daily for 2 days, 48 hours, During CM administration After CM administration	
Aslanger, 2012 [6] (continued)				3	Ia nac	Other, IA	600mg IA before procedure, 1200mg by mouth twice daily for 2 days, 48 hours, Prior to CM administration After CM administration	
				2	Nac	Oral	600mg, 72 hours, Prior to CM administration During CM administration After CM administration	2 doses prior to procedure, 2 doses day of procedure, 1 dose after procedure
Bader,2004 [7]	Iohexol, Iopromide, LOCM	IA	Arm 1:mean 217ml Arm 2 mean 205ml Dose/duration not specified	1	Saline infusion before and after procedure	IV	2000ml/24hours, 12h before and 12h after, Prior to CM administration After CM administration. All patients allowed oral hydration after procedure.	Total volume of saline=2000mls. Type of saline not specified.
				2	Saline infusion during procedure	IV	300ml bolus, Bolus during procedure, During CM administration . All patients allowed oral hydration after procedure.	300mls bolus. Type of saline not specified.

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Baskurt, 2009[8]	LOCM, Other description, Ioversol	IA	Not specified	1	Hydration	IV	1 ml /kg/ h for 12 h before and after contrast exposure, 12 h before and after contrast exposure, Prior to CM administration After CM administration	
				2	Hydration + N-acetylcysteine	Oral, IV	1 ml /kg/ h of Isotonic Saline for 12 h before and after contrast exposure + NAC: 600 mg p.o. Twice daily the preceding day and the day of angiography, 12 h before and after contrast exposure, Prior to CM administration	
				3	Hydration + N-acetylcysteine + theophylline	Oral, IV	1 ml /kg/ h of isotonic saline for 12 h before and after contrast exposure.NAC + theophylline (600 mg NAC p.o. And 200 mg theophylline p.o. Twice daily for the preceding day and the day of angiography, 12 h before and after contrast exposure, Prior to CM administration	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Briguori, 2004 [9]	Iodixanol,	IA	Not specified, Define, Mean: Arm1 160 (SD 82), Arm2 168ml (SD 104)	1	0	NR		
				2	NAC + saline	Oral, IV	0.45% saline 1ml/kg, 1,200mg NAC twice daily = 4800mg total, 48 hours, Prior to CM administration During CM administration After CM administration	Saline given before and after procedure, NAC given day before and day of procedure
				3	Fenoldopam mesylate + saline	Oral, IV	0.45% saline 1ml/kg, Fenoldopam given at 0.10 ug/kg/min, 24 hours, Prior to CM administration During CM administration After CM administration	Saline given before and after procedure, Fenoldopam started 1 hour before procedure and continued through till 12 hours after.
Briguori, 2004[10]	Other description, Iobitriolol	IA	Not specified, Mean: Arm2 184ml (SD 122), Arm3 174 ml (SD 108)	1	0			All pts had saline 0.45% 1/ml/kg 12h before-12h after CM
				2	NAC single dose	Oral	NAC 600g bid, 2 days, Prior to CM administration After CM administration	1 day before-1 day after CM
				3	NAC double dose	Oral	NAC 1200 mg bid, 2 days, Prior to CM administration After CM administration	1 day before-1 day after CM
Briguori, 2007[11]	Iodixanol	IA	Dose and duration not specified. Mean volume: Arm 1: 179ml, Arm 2: 169ml, Arm 3: 169ml	1	IV Normal Saline + oral NAC	Oral, IV	IV 0.9% saline, 1ml/kg/hr, 12 hours before and 12 horus after contrast media administration. NAC given at 1200mg twice daily the day before and day after procedure.	All patients given Arm 1 intervention.
				2	IV NaHCO3 + oral NAC	Oral, IV	154mEq/L sodium bicarbonate in dextrose and water. Initial bolus 3ml/kg/hr given 1 hour before contrast media, 1ml/kg/hr during procedure and for 6 horus after.	All patients given Arm 1 intervention, along with sodium bicarbonate.
				3	IV Normal Saline + IV ascorbic acid + oral NAC	Oral, IV	3g of ascorbic acid IV 2 horus before contrast media, and received 2g the night and morning after procedure.	All patients given Arm 1 intervention, along with ascorbic acid.

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Briguori, 2011 [12]	Iodixanol	IA	Not specified	1	IV Sodium bicarbonate + oral NAC	Oral, IV	IV 154 meq/L sodium bicarbonate, 1200mg NAC twice daily for 2 days, 7 hours sodium bicarbonate, 2 days NAC, Prior to CM administration During CM administration After CM administration	
				2	RenalGuard: IV 0.9% saline + IV NAC + RenalGuard System + IV furosemide	Oral, IV	Furosemide 0.25 mg/kg, NAC 1500mg, ~ 8 hours, Prior to CM administration During CM administration After CM administration	Includes hydration with 0.9% saline and use of renalguard system. Renalguard system includes a closed-loop fluid management system, a high-volume fluid pump, a high-accuracy dual weight measuring system, motion-detection artifact reduction, a single-use intravenous set and urine collection system that interfaces with a standard Foley catheter, real-time display of urine and replacement fluid volume, timely alerts to drain the urine bag or to replace the hydration fluid bag, and safety features such as automatic air and occlusion detection.
Chen, 2008[13]	IOCM	IA	mean 285 +/- 107 (for both groups with normal renal function), 298 +/- 125 (for both groups with abnormal renal function), Not specified	1	Normal renal function-Non hydration	Other, usual care	NR	Non-hydration intervention not specified
				2	Normal renal function-0.45% saline	IV	Saline 0.45% 1ml/kg/h, 18h, Prior to CM administration After CM administration	
				3	Abnormal renal function-NAC+Non hydration	Oral	NAC 1200 mg bid, 18h, Prior to CM administration After CM administration	Non-hydration intervention not specified
				4	Abnormal renal function-NAC+-0.45% saline	Oral, IV	NAC 1200 mg bid + Saline 0.45% 1ml/kg/h, 18h, Prior to CM administration After CM administration	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Cho, 2010 [14]	Isoversol	IA	320mg iodine/ml, duration not specified, 118-136 ml	1	IV 0.9% saline	IV	Saline infusion3ml/kg/h 1 h pre - 1ml/kg/h 6 h after, 7H, Prior to CM administration During CM administration After CM administration	154 meq, normal saline
				2	IV sodium bicarb + IV 0.9% saline	IV	Sodium bicarb infusion3ml/kg/h 1 h pre - 1ml/kg/h 6 h after, 7H, Prior to CM administration During CM administration After CM administration	154 meq
				3	Oral fluids (water)	Oral	Water 500 ml 4 h before procedure stop 2 h prior + 600 ml after procedure, 2H, Prior to CM administration After CM administration	
				4	Oral fluids (water) + oral bicarb	Oral	Water 500 ml 4 h before procedure- stop 2 h prior + 3.9g sodium bicarb oral 20 min before procedure +600 ml after procedure, 2H, Prior to CM administration After CM administration	46.4 meq
Demir, 2008 [15]	Iomeprol, Iopamidol	IV	100ml: Iomeprol (61.25 g/ml) Iopamidol (61.25 g/ml), Not specified, Define, 100ml: Iomeprol (61.25 g/ml) Iopamidol (61.25 g/ml)	1	Saline	IV	2000ml 0.9% saline hydration, 48 hours (24 pre and 24 post), and after CM administration	Normal saline given to all arms
				2	Saline +NAC (NAC)	Oral	Hydration as arm 1 + NAC 600 ml/d, 3 days prior, day of, 1 day post procedure	In the morning plus control
				3	Saline + Misoprostol (M)	Oral	Hydration as arm 1 + misoprostol 400 mg/d (200mg, 2x/day), 3 days prior, day of, 1 day post CM	Plus control
Demir, 2008 [15]				4	Saline + Theophylline (T)	Oral	Hydration as arm 1 + theophylline 200mg/d, 3 days prior, day of, 1 day post CM	In the morning plus control
				5	Saline + Nifedipine (N)	oral	Hydration as arm 1 + nifedipine 30 mg/day, 3 days prior, day of, 1 day post CM	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Durham, 2002[60]	Iohexol	IA	Mean: Arm1 48.1 min (SD 30.9), Arm2 44.8 min (SD 19.1), Define, Mean: Arm1 84.7 ml, Arm2 77.4 ml	1	IV hydration plus placebo	Oral	Saline 0.45% 1 ml/kg/h, placebo NR, 1h before and 3h after, Prior to CM administration After CM administration	Saline hydration given for 12 hours before and and up to 12 hours after procedure All patients were placed on conventional iv hydration but actual rate and duration was left to physician
				2	IV hydration plus NAC	Oral	Saline 0.45% 1 ml/kg/h, 1200mg NAC, 1h before and 3h after, Prior to CM administration After CM administration	Saline hydration given for 12 hours before and and up to 12 hours after procedure
Erol, 2013 [16]	Iohexol	IA	780mosm/kg +50mg iodine/mL, Not specified	1	Saline hydration	IV	1 mg/kg/h normal saline, 24 hours, Prior to CM administration After CM administration	12 hours pre and 12 hours post contrast
				2	Saline hydration + alloprinol	Oral, IV	300mg allopurinol + 1 mg/kg/h normal saline, 24 hours, Prior to CM administration After CM administration	Allopurinol 24 hours before+ hydration: 12 hours pre and 12 hours post contrast
Firouzi, 2012[17]	Iodixanol, Iopromide	IA	325.34(101.41) vs 319.28(98.1) p=0.6	1	Control	NR	Normal Saline	
				2	Pentoxifylline	IV	Hydration as arm 1 + pentoxifylline 400mg 3xd for 2 days	
Frank, 2003[18]	Iomeprol	IA	mean dose was 80 mL; 3 CM injections into LCA and 2 injections into the RCA + biplane levocardiography using 25 mL	1	0.9% saline volume expansion	IV	1000 ml 0.9% saline, 12 Hours. Prior and After CM administration	6 hours pre and 6 hours post CM admin
				2	0.9% saline voume expansion + high-flux HD	control + HD	1000 ml 0.9% saline (same as control) + HD, saline duration was the same as in the control group; HD was over 4 hours during CM admin. Prior and After CM administration	Plus control regimen

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Gu, 2013 [19]	Not specified	IA	Not specified	1	Control--saline	IV	1ml/kg/hr saline, From 4 hours before to 24 hours after surgery, Prior to CM administration During CM administration After CM administration	New York Heart Association stage 2 and 3 had limited oral intake of fluids
				2	Furosemide	IV	20mg furosemide, over 30 seconds 7-13 minutes (~10.1 +/- 3.2 min) after procedure, After CM administration	This group also received same saline protocol as control
Gulel, 2005 [63]	Ioxaglate	IA	Not specified, Not specified	1	Control	NR		All patients received saline 1ml/kg/h infusion 12 h before-12 h after CM
				2	Nac	Oral	600mg bid, 2days, Prior to CM administration After CM administration	The day before and the day of the day of CM
Gunebakmaz, 2012[20]	Iopromide, LOCm	IA	61-64, Not specified, Not specified	1	Saline	IV	1ml/kg/h, 18 hours, staring 12 hours before the procedure, Prior, during and after CM administration	0.9% saline for all arms
				2	Saline + nebivolol	NR	600mg bid, 4 days, starting 2 days before the procedure, Prior, during and after CM administration	
				3	Saline + NAC	IV	5mg day, 4 days, starting 2 days before the procedure, Prior, during and after CM administration	
Hafiz, 2012 [21]	LOCM	IA	Not specified, Not specified	2	NS with or without NAC	Oral, IV	0.9% saline 1ml/kg, 1200mg NAC administered twice, 2400mg total, 24 hours saline, Prior to CM administration After CM administration	NAC administered 2-12 hours before procedure and 6-12 hours after procedure
				3	Sodium Bicarbonate with or without NAC	Oral, IV	154 meq/l NAHCO3 3ml/kg/hour, 1200mg NAC administered twice, 2400mg total, 7 hours NAHCO3, Prior to CM administration After CM administration	NAC administered 2-12 hours before procedure and 6-12 hours after procedure

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Hans,1998[22]	Iohexol, Other description, the brand is Omnipaque 300 (concentration is listed below under dose)	IA	OMNIPAQUE 300 contains 647 mg of iohexol equivalent to 300 mg of organic iodine per mL (per package insert), Not specified, Define, 140 ml (SD=29.6) for control group and 146 mls (SD=46) for dopamine group	1	Placebo	IV	NR, Does not specifically say, but may also be 12 hours (see below), Not stated	Article says that patients in the control group received an equal volume of normal saline. The timing is not stated. It may be the same timing as the dopamine, but it does not explicitly say Patients were encouraged to drink liquids before and after the arteriography (assumption is that this means all patients).
				2	Dopamine	IV	2.5 mcg/kg/min of dopamine, 12 hours, Prior to CM administration During CM administration After CM administration	It seems that the dopamine is continued during the contrast administration also (does not say it was stopped during that time, so it sounds like it is given prior, during, and after CM administration)
Hashemi, 2005 [23]	Other description, Meglumin compound	IA	370 mg/ 20ml, Define, 2 hours prior procedure to 48 hours after, Define, Mean: Arm1 223.3ml (SD 130), Arm2 225ml (SD 120)	1	Placebo	Oral	Placebo NR, 2 hours prior to procedure until 48 hours after procedure	All the patients had received aspirin 100 mg/d and ticlopidin 250 mg/bid from one week prior to angioplasty, and normal saline 0.9% infusion (total volume of 1.5 liter) at a rate of 60 ml/hr from 12 hours before angioplasty until 12 hours after the procedure.
				2	Captopril	Oral	12.5mg captopril every 8 years, 2 hours prior to procedure until 48 hours after procedure, Prior to CM administration During CM administration After CM administration	
Heguilen, 2013 [24]	Ioversal	NR	Dose: 678mg/dose, duration not specified. Mean Volume: Arm2 179.8ml, Arm3 209.9 ml, Arm4 186.6ml	1	Sodium bicarbonate	IV	154 mmol nahco3, at 3ml/kg, 15 hours, Prior to CM administration During CM administration After CM administration	All arms fluid mixed with 5% dextrose

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Heguilen, 2013 [24] (continued)				2	NAC+NaHCO3	Oral, IV	600mg NAC, twice daily., 2 days, Prior to CM administration During CM administration	
				3	NAC + NaCl	Oral, IV	600mg NAC plus 154 mmol nacl solution at 3ml/kg/h, 2 days, Prior to CM administration During CM administration After CM administration	Saline solution given 2 hours before procedure and 12 hours after. NAC given in same schedule as Arm3
Holscher, 2008[25]	Iopromide	NR	Not specified	1	Hydration only	IV	500 ml 5% glucose and 500 ml 0.9% sodium chloride, 12h before and after, Prior to CM administration After CM administration	
				2	Hydration plus dialysis	IV	500 ml 5% glucose and 500 ml 0.9% sodium chloride, 12h before and after, Prior to CM administration After CM administration	
				3	Hydration plus NAC	Oral, IV	500 ml 5% glucose and 500 ml 0.9% sodium chloride plus 600mg NAC, NR, Prior to CM administration After CM administration	
Huber, 2006[26]	Iomeprol, Other description, Imeron	IA and IV	Not specified, Define, 100-400ml	1	0			
				2	Theophylline	IV	200 mg infusion 30 min before CM, short infusion, Prior to CM administration	Started 30min before contrast procedure. Hydration for all arms dependent on physician and patient condition.
				3	Acetylcysteine	IV	600 bid, 2 days, day before and day of procedure, Prior to CM administration During CM administration	Starting the day before. Hydration for all arms dependent on physician and patient condition.
				4	Theophylline + acetylcysteine	IV	200 mg infusion 30 min before CM, 600mg bid of acetyl, 2 days, day before and day of procedure, Prior to CM administration	Starting the day before. Hydration for all arms dependent on physician and patient condition.

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Kimmel, 2008[27]	Iomeprol	IA	Not specified	1	Placebo	Oral	NR, 48 hours, Prior to CM administration During CM administration	Day before and day of procedure All patients received a peri-procedural intravenous infusion ('volume expansion') of 1 ml/kg/h with 0.45% saline for 24 h (12 h before and 12 h after exposure to CM)
				2	Nac	Oral	600mg b.i.d, 48 hours, Prior to CM administration During CM administration	Day before and day of procedure
				3	Zinc	Oral	60mg daily, 24 hours, Prior to CM administration	Day before
Kinbara, 2010[28]	Iopamidol,	IA	0.755g/ml	1	Hydration	IV	1ml/kg/hr, 30min before and 10hrs after angiography, prior and after CM administration	Arm 2: NAC and Arm 3: Aminophylline
				2	Hydration and aminophylline	IV	250mg +control treatment, 30min before+control treatment, Prior to CM administration	
				3	Hydration and N-acetylcysteine	Oral	704mg twice daily+control treatment, day before and during procedure+control, prior and during CM administration	
Klima, 2012 [29]	LOCM, IOCM	IA or IV	Not specified	1	0.9% saline	IV	0.9% saline, 1 ml/kg/h, ~20 hours, Prior to CM administration During CM administration After CM administration	Saline started at 8pm day before procedure and for at least 12 hours after procedure
				2	Long term sodium bicarbonate	IV	166 meq/L, ~8 hours, Prior to CM administration During CM administration After CM administration	Sodium bicarbonate given for 1 hour before CM administration during CM administration and 6 hours after procedure
				3	Short term sodium bicarbonate	Oral, IV	166 meq/L + 500mg, 20 min, Prior to CM administration During CM administration	Given 20 min sodium bicarbonate through IV, and then 500mg sodium bicarbonate orally at start of infusion

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Koc, 2012[30]	Iohexol	IA	Dose and duration not specified. Volume Mean: Arm1 130ml, Arm2 130ml, Arm3 120ml	1	IV 0.9% saline	IV	0.9% saline 1 ml/kg/, 12 hours before and 12 hours after the coronary procedure, Prior to CM administration After CM administration	
				2	IV NAC plus high-dose IV 0.9% saline	IV	IV bolus of 600 mg of NAC twice daily, before and on the day of the coronary procedure, Prior to CM administration During CM administration After CM administration	IV 0.9% saline 1 ml/ kg/h before, on and after the day of the coronary procedure
				3	IV 0.9% saline	IV	IV 0.9% saline 1 ml/kg/, before, on and after the day of coronary procedure, Prior to CM administration During CM administration After CM administration	
Kong, 2012 [31]	Iopromide	IA	Not specified	1	IV 0.9% saline	IV	12 hrs before the procedure and continued for 24 hrs after procedure, Prior to CM administration During CM administration After CM administration	Normal saline, 1ml/kg/hr Duration is difficult to describe and details are under dose
				2	Oral hydration before and after procedure	Oral	500 ml 2 hrs before procedure and 2000 ml within 24 hrs following procedure, Prior to CM administration After CM administration	Tap water
				3	Oral hydration after procedure	Oral	2000 ml within 24 hrs following procedure, After CM administration	Tap water

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Kotlyar, 2005[32]	Iopromide, Other description, Ultravist-370, 0.769 mg/ml, 370mg iodine/ml; Schering Berlin, Germany	IA	Not specified, Define, mean 87ml in Arm 1, mean 89 ml in Arm 2 and mean 86ml in Arm 3	1	IV hydration	IV	0.9% saline commenced at 200 ml/h 2 h before angiography and continued for a further 5 h after the procedure, NR, Prior to CM administration After CM administration	All patients, scheduled for angiography, received written instruction to drink 1 l of fluid the evening prior to the procedure
				2	NAC 300mg	Oral	IV NAC 300mg +IV Hydration0.9% saline (Nacl at 200 ml/h 2 h before angiography and continued for a further 5 h after the procedure), NR, Prior to CM administration After CM administration	NAC was prepared in 100 ml of 5% dextrose and administered over 20 min, 1–2 h before angiography and again 2–4 h after angiography
				3	NAC 600mg	Oral	IV NAC 600mg +IV hydration0.9% saline (Nacl at 200 ml/h 2 h before angiography and continued for a further 5 h after the procedure), NR, Prior to CM administration After CM administration	NAC was prepared in 100 ml of 5% dextrose and administered over 20 min, 1–2 h before angiography and again 2–4 h after angiography
Krasuski, 2003[33]	Not specified	IA	Arm 1 mean=1.7cc/kg; Arm 2 mean 1.6cc/kg Arm 1 mean=136cc; Arm 2 mean=131cc	1	Overnight hydration dextrose plus saline	IV	5% dextrose in half normal saline - 1cc/kg/h, 12h before. Prior to cm administration	Upon completion of the study, all patients were encouraged to take oral fluids and received 12 hours of iv 5% dextrose in half normal saline at 1cc/kg/hr
				2	Bolus normal saline	IV	Bolus-250cc normal saline, 20mins. Prior to CM administration	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Lawlor, 2007 [34]	Not specified	IA	100-200mg, Not specified, Define, Arm 1 mean=163ml; Arm 2 mean=158; Arm 3 mean=165ml	1	Iv 0.9% saline	Oral, IV	IV 0.9 nacl 1 ml/kg/hr+ placebo(3 ml of 0.9% nacl in 30 ml of ginger ale), 112 hr of IV hydration before and after, Prior to CM administration After CM administration	Placebo given at same time as NAC was given to Arm 2 Unlimited oral hydration was encouraged in the postprocedure period in all groups
				2	Iv 0.9% saline + nac	Oral, IV	600 mg NAC in 30 ml of ginger ale orally twice daily the day prior to and the day of angiography and 12 hr of IV hydration (0.9 nacl 1 ml/kg/hr) both prior to and following the procedure, 48hours, Prior to CM administration	
				3	Oral hydration+nac	Oral	NAC (600 mg in 30 ml of ginger ale orally twice daily the day prior to and the day of angiography)+outpatient oral hydration preparation of 1,000 ml water in the 12 hr prior to the procedure + followed by IV hydration (0.9 nacl 1 ml/kg/hr) beginning 1-2 hr prior to the procedure and continuing for a total of 6 hr afterward, Prior to CM administration	
Lehnert, 1998 [61]	, Iopentol, Other description, the concentration of the iopentol: 350 mg iodine/mL = 810 mOs/kg H2O)	IA and IV	3.0ml/kg(SD=0.4) for control and 3.5 ml/kg(SD=0.6) for the hemodialysis group, Not specified	1	Conservative treatment	IV	0.9% saline at 83 ml/hour, 24 hours (IVF beginning 12 hrs before contrast, then continued at the same rate for 12 hours after contrast), Prior to CM administration After CM administration	All patients received 0.9% saline as described. If the patient was not on a calcium channel blocker, then 10 mg nitrendipine per 12 hours was scheduled beginning 12 hours before catheterization (? Duration). Arm 1: IVF + oral Ca blocker if not on one (see above) Arm 2: IVF + HD + oral Ca blocker if not one one (see above)

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Lehnert, 1998 [61] (continued)				2	Hemodialysis	Other, Vascular accces shaldon catheter (femoral vein)	High flux polysulphone membrane, average blood flow 139 +/- 8 ml/min, dialysate flow 500 ml/min. No fluid withdrawal., 3 hours (also 24 hours of IVF as in the control group), After CM administration	All patients received 0.9% saline as described in Arm 1. If the patient was not on a calcium channel blocker, then 10 mg nitrendipine per 12 hours was scheduled beginning 12 hours before catheterization. Dialysis was started as soon as possible after termination of contrast (mean 63 +/- 6 min)
Li, 2011[36]	Not specified	IA	Not specified	1	Control	NR	Normal Saline	Saline 1ml/kg/h infusion 6 h before- 6 h after All patients had 2 weeks washout for all ACEI before starting the trial
				2	Benazepril	Oral	Benazepril 10mg/day, 3 days, Prior to CM administration	Normal saline 1ml/kg/h infusion 6 h before- 6 h after
Li,2009 [35]	Iohexol	IA	Not specified, Define, 121 +/- 56 for arm 1, 116 +/- 65 for arm 2	1	Control	NR	Normal Saline	Saline 1ml/kg/h infusion for 12 h after CM
				2	Probucol	Oral	Probubol 500mg bid, 3d before and after procedure	Saline 1ml/kg/h infusion for 12 h after CM
Ludwig, 2011 [37]	Iomeprol	IA	Not specified, Define, 120-200 (comparable in both arms	1	Control	IV	Placebo before CM, NS, Prior to CM administration During CM administration After CM administration	Plus nacl 1000 ml before and 500 ml after
				2	Mesna	IV	1600 mg MESNA before CM, NS (pulse regime), Prior to CM administration During CM administration After CM administration	Plus nacl 1000 ml before and 500 ml after

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Maioli, 2008[38]	IOCM	IA	Not specified	1	IV Isotonic Saline plus oral NAC	IV, Oral	1ml/kg/h 0.9% Sodium Chloride plus oral NAC 600mg, twice day, 12h. Prior and After CM administration	The two arms also got oral NAC 600mg, twice daily, day before and day after the procedure in addition to the IV saline versus bicarbonate.
				2	IV Sodium Bicarbonate plus oral NAC	IV, Oral	1ml/kg/h 0.9% Sodium Chloride plus oral NAC 600mg, twice day, 1h, 6h. Prior and After CM administration	
Maioli, 2011 [39]	Iodixanol, IOCM	IA	Dose and duration not specified. Mean Volume: Arm1 224ml, Arm2 216 ml. Arm3 208ml	1	No hydration	No hydration	Not stated	
				2	Late 0.9% saline	IV	1ml/kg 0.9% saline solution, 12, After CM administration	
				3	Early sodium bicarbonate	IV	3ml/kg, 154 meq/L sodium bicarbonate, for 1 hour before and 12 hours after PCI, Prior to CM administration During CM administration After CM administration	
Marenzi, 2006 [40]	Iohexol, LOCM, Other description, 350 mg of iodine per milliliter; Omnipaque, Amersham Health	NR	Define, Arm 1 mean 274;Arm 2mean= 264;Arm 3 mean= 253	1	Placebo	Other, NR		All treated patients and control patients underwent hydration with in-travenous isotonic saline (0.9 percent) at a rate of 1 ml per kilogram of body weight per hour (or 0.5 ml per kilogram per hour in cases of overt heart failure) for 12 hours
				2	Standard dose NAC	Oral, IV	Total dose of 3000mg, Prior to CM administration After CM administration	Intravenous bolus of 600 mg of N-acetylcysteine before primary angioplasty and a 600-mg tablet orally twice daily for the 48 hours after intervention
				3	High dose NAC		Total dose of 6000mg, Prior to CM administration After CM administration	Intravenous bolus of 1200 mg of N-acetylcysteine before intervention and 1200 mg orally twice daily for the 48 hours after intervention

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Marenzi, 2012 [41]	Iomeprol	IA	Not specified, Define, comparable between groups	1	Saline hydration	IV	Saline 0.9%1 ml/kg/h (0.5 ml/kg/h in case of left ventricular ejection fraction < 40%, 24 h infusion- 12h before and 12h after, Prior to CM administration After CM administration	Saline for all arms
				2	Furosemide plus matched hydration	IV	Furosemide- single IV bolus of 0.5 mg/kg (up to a max of 50 mg), over 30 min, Prior to CM administration Saline infusion 90mins before and up to 4hrs after	Saline infusion 90mins before and up to 4hrs after
Marron, 2007[42]	Iodixanol	IA	Not specified	1	Isotonic 0.9% saline	IV	, 12h before and 12h after, Prior to CM administration After CM administration	Volume of iv fluid=2000mls in total
				2	Hypotonic 0.45% saline	IV	, 12h before and 12h after, Prior to CM administration After CM administration	
Mehran, 2009[64]	Iodixanol, Ioxaglate	IV	Not specified	1	0	IV	Diphenydramine 25 mg IV before and IV one-half isotonic saline at 100 ml/h for 3-5 hours and for 12 hrs after CM administration During CM administration	N-acetylcysteine administered at discretion of investigator
				2	Iodixanol	IV	Diphenydramine 25 mg IV before and IV one-half isotonic saline at 100 ml/h for 3-5 hours and for 12 hrs after CM administration During CM administration	N-acetylcysteine administered at discretion of investigator
				3	Ioxaglate			
Mohamed,2008 [65]	Iohexol, LOCM	IA	Not specified, Define, Arm 1 mean(SD)=126.67(94.37) ml; Arm 2 mean (SD)=136.73 (100.23)ml	1	IV hydration	IV	Saline (0.45% NS) was given intravenously at a rate of I ml/kg/h 12 hours before and after coronary angiogram, 24h, Prior to CM administration After CM administration	
				2	IV hydration + oral NAC	Oral, IV	Oral NAC 600mg twice daily for four doses starting 12 hours before procedure + Saline (0.45% NS) was given intravenously at a rate of I ml/kg/h 12 hours before and after coronary angiogram, 24h, Prior to CM administration After CM administration	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Mueller,2002 [43]	LOCM, Other description, Ultravist 370; Schering, Berlin, Germany; and Imeron 350; Byk Gulden, Konstanz, Germany	IA	Dose and duration not specified. Mean Volume: Arm 1mean=232ml; Arm 2 mean=236ml	1	Isotonic Saline hydration	IV	1ml/kg of 0.9% saline, 24h, Prior to CM administration During CM administration After CM administration	Sodium concentration of 154mmol/l
				2	.45% sodium chloride plus 5% glucose	IV	1ml/kg of 0.45% sodium chloride plus 5% glucose, 24h, Prior to CM administration During CM administration After CM administration	Sodium concentration of 77mmol/l
Ng, 2006 [44]	Iodixanol, Iohexol, Ioxaglate	IA	Not specified, Define, 172.2 +/- 73.2 NAC group, 164.4 +/- 85.0 fenoldopam group	1	Hydration	IV	normal saline 1ml/kg/h, 1-2 h before CM and for 6-12 h after CM	All pts received hydration with normal saline
				2	Nac	Oral	NAC 600mg bid 4 doses, 2days, Prior and after CM administration	3 doses before CM - 1 dose after CM
				3	Fenoldopam	IV	0.1 mcg/kg/min, 8h, , during and after CM administration	Infusion started 2 h before CM
Oguzhan, 2013[45]	Iopromide	IA	Not specified	1	AVH (amlodipine valsartan hydration group)	Oral, IV	5/160 mg; 1ml/kg/hr, amlopidine/valsartan was given in 3 doses- one dose 24 h before the procedure, second on the morning before and third dose was given 24 hr aftrer contrast media exposure. Hydration therapy with isotonic nacl was administered 12 h before and after contrast media exposure, both arm recieved hydration, prior and after cm administration	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Oguzhan, 2013[45] (continued)				2	H (hydration group)	IV	1ml/kg/hr, Hydration therapy with isotonic NACL was administered 12 h before and after contrast media exposure, both arms recieved hydration, Prior and after CM administration	
Ozhan, 2010[46]	Iopamidol	IA	Not specified, Define, comparable between groups	2	Nac	Oral	NAC 600 mg twice daily, day after procedure, 1 day, After CM administration	Saline 1000 ml infusion for 6 h after procedure. Saline not specified.
				3	Nac + atorvastatin	Oral	NAC 600 mg and Atorvastatin 80 mg twice daily on day 1 after procedure. Atorv 80mg d for 2 days after procedure, 3 days, After CM administration	Saline 1000 ml infusion for 6 h after procedure. Saline not specified.
Pakfetrat, 2009[47]	IOCM (Iodixanol)	IA	Not specified	1	Sodium chloride	IV	1ml/kg/hr normal saline in 5% dextrose, 6hrs before and 6hrs after. Prior and after cm administration	
				2	Sodium bicarbonate in dextrose solution	IV	3ml/kg/hr before and 1ml/kg/hr after, 1hr before and 6hrs after. Prior and after cm administration	
				3	Sodium chloride plus oral Acetazolamide	IV	250mg, 2hrs before and 6hrs after. Prior and after cm administration	
Ratcliffe, 2009 [48]	Iodixanol, IOCM, Other description, nonionic 320 mg iodine/mL; 290 mOsm/kg water [Visipaque, GE Healthcare, USA	IA	Dose and duration not specified, Mean Volume; Arm 1mean=131, arm 2 mean=175, Arm 3 mean 169, arm 4 mean =125	1	IV normal saline	IV	Nacl (154 meq/L nacl in 5% dextrose), at an infusion rate of 3 ml/kg/h for 1 h before contrast, and continued at 1 ml/kg/h during the procedure and for 6 h following contrast exposure., 7h, Prior to CM administration During CM administration After CM administration	All patients given saline or sodium bicarbonate in 5% dextrose.

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Ratcliffe, 2009 [48] (continued)				2	IV normal saline + IV/oral NAC	Oral, IV	IV bolus of 1200 mg of NAC 1 h before intervention and 1200 mg orally twice daily for 48 h after intervention + IV nacl (154 meq/L nacl in 5% dextrose), at an infusion rate of 3 ml/kg/h for 1 h before contrast, and continued at 1 ml/kg/h during the procedure and for 6 h following contrast exposure, 2 days, Prior to CM administration During CM administration After CM administration	
Ratcliffe, 2009 [48] (continued)				3	IV NaHCO3	IV	IV nahco3 (154 ml of 1000 meq/L nahco3 to 846 ml of 5% dextrose, slightly diluting the dextrose concentration to 4.23%) at an infusion rate of 3 ml/kg/h for 1 h before contrast, and continued at 1 ml/kg/h during the procedure and for 6 h following contrast exposure., 7h, Prior to CM administration During CM administration After CM administration	
				4	IV NaHCO3+ IV/oral NAC	Oral, IV	IV bolus of 1200 mg of NAC 1 h before intervention and 1200 mg orally twice daily for 48 h after intervention + nahco3 (154 ml of 1000 meq/L nahco3 to 846 ml of 5% dextrose, slightly diluting the dextrose concentration to 4.23%) at an infusion rate of 3 ml/kg/h for 1 h before contrast, and continued at 1 ml/kg/h during the procedure and for 6 h following contrast exposure, 2 days, Prior to CM administration During CM administration After CM administration	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Recio-Mayoral, 2007 [49]	Iomeprol, LOCM, Other description, Iomeron, Bracco s.p.a, Milan, Italy) with 350 mg/ml of iodine content	IA	Not specified, Define, Arm 1 mean+/-SD=279+/-94; Arm 2=290+/-114ml	1	Saline + NAC after procedure	Oral, IV	IV isotonic saline (0.9%) at rate of 1 ml/kg/h for 12 h after PCI + 2 doses of 600 mg NAC orally the next day, 24h, After CM administration	Standard institution protocol is perfusion with isotonic saline (0.9%) at rate of 1 ml/kg/h for 12 h after PCI
				2	IV Bolus+ NAC before procedure +NAC after procedure	IV	2400mg NAC in an IV bolus solutionof 5 ml/kg/h of alkaline saline with 154 meq/l of sodium bicarbonate in 5% glucose and H2O (adding 77 ml of 1,000 meq/l sodium bicarbonate to 433 ml of 5% glucose in H2O) over 1 hr, in the 60 mins before contrast + 1.5 ml/kg/h fluid therapy in the 12 h after the procedure + 2 doses of 600 mg NAC orally the next day, 24h, Prior to CM administration After CM administration	
Reinecke, 2007 [50]	Iopromide, IOCM, Other description, (Ultravist 370TM, Schering AG, Berlin, Germany).	NR	Arm1:mean 188; Arm 2 mean184; Arm3 mean197mg/dl, Not specified	1	Hydration only	IV	Glucose 5% + Saline 0.9% 24 h (1000 ml 12 h before- 1000ml 12 h after CM)	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Reinecke, 2007 [50] (continued)				2	Hydration + dialysis	IV, Other, hemodialysis	Glucose 5% + Saline 0.9% 24 h (1000 ml 12 h before- 1000ml 12 h after CM) Low-flux HD started within 20 min after procedure for 2 hours	
				3	Hydration + NAC	Oral, IV	Glucose 5% + Saline 0.9% 24 h (1000 ml 12 h before- 1000ml 12 h after CM) NAC 600 mg x4 (2 doses before and after)	One dose NAC 600 mg was given at the evening before catheterization, the second dose was given on the morning before catheterization; the third was given at the evening after catheterization and the last dose was given on the morning the day after angiography.
Rosenstock, 2008 [51]	IOCM, Not specified, Other description, 95% IOCM other 5% not specified	IA	Not specified, Define, Arm 1 125 +/- 75, arm 2 142 ± 76, arm 3 149 ± 90	1	Naive to angiotensin blockade	Other, No prior use of angiotensin blockade	N/a	79% had acetylcysteine+hydration(71%, 1/2 normal, 32% normal) Metformin and diuretics were withheld in all patients
				2	Continue angiotensin blockade during and after procedure	Other, Angiotensin blockade continued during and after procedure	N/a	74% had acetylcysteine(68%, 1/2 normal, 20% normal)
				3	Discontinue angiotensine blockade morning of procedure and 24hrs after procedure	Other, angiotensin blockade stopped morning of procedure and 24hrs after procedure	N/a	78% had acetylcysteine+hydration(79%, 1/2 normal, 27% normal)

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Seyon, 2007[66]	Iohexol	IA	147.5+/- 74.5 ml (tc); 133.68+/-58.04 (control)	1	Placebo+hydration	Oral	Placebo similar to NAC, once before procedure and then twice daily after for total of 4 doses. Prior and After CM administration	IV saline 0.45% 1 ml/kg/hr; 4-6 hours pre and 12 hours post
				2	N-Acetylcysteine+hydration	Oral	600mg, once before procedure and then twicw daily after for total of 4 doses. Prior and after cm administration	Iv saline 0.45% 1 ml/kg/hr; 4-6 hours pre and 12 hours post
Shavit, 2009 [67]	Iopamidol	NR	755 mg iopamidol per milliliter, and 370 mg iodine per milliliter, Not specified	1	Sodium bicarbonate	IV	154 meq/L sodium bicarbonate in 5% dextrose.The initial IV bolus was 3 ml/kg for 1 hour before cardiac catheterization. Following this bolus, patients received the same fluid at a rate of 1 ml/kg per hour during the contrast exposure and for 6 hours after the procedure, Prior to CM administration During CM administration After CM administration	Bolus 3mefore procedure followed by infusion lml/kg/h for 12 hours Both arms 154 meq
				2	Sodium chloride + nac	Oral, IV	NAC 600 mg× 2/d PO the day before and the day of the procedure., 2d, Prior to CM administration	12-hour infusion 1 ml/kg/h before cardiac catheterization
Shemirani, 2012 [62]	Other description, meglumine	IA	Not specified, Define, 120 ± 40 group a; 115 ± 57 group b; 133 ± 70 group c; 119 ± 42 group d	1	0			All patients received normal saline (0/9%) in a dose of 1 ml/kg/h 12 h before and 24 h after PCI
				2	Prior use of captopril then discontinued 36hrs before procedure	Oral	Not specified. About 36hrs before PCI, drug discontinued, 36hrs before PCI, drug discontinued, Prior to CM administration	
				3	Prior use of captopril continued during procedure	Oral	Not specified, Continued during procedure, Prior to CM administration During CM administration	
				4	Prior use of furosemide then discontinued 36hrs before procedure	Oral	Not specified. About 36hrs before PCI, drug discontinued, 36hrs before PCI, drug discontinued, Prior to CM administration	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Shemirani, 2012 [62] (continued)				5	Prior use of furosemide continued during procedure	Oral	Not specified, Continued during procedure, Prior to CM administration During CM administration	
Solomon, 1994[53]	32% ionic high osm /32% ioinic low osm / 35% non ionic low osm	IA	Not specified	1	Saline	IV	1/ml/kg, 24 hours. Prior, during and after cm administration	Saline 0.45%
				2	Mannitol + saline	IV	25 mg, 60 minutes. Prior to cm administration	Saline 0.45%
				3	Furosemide + saline	IV	80 mg, 30 minutes. Prior to cm administration	Saline 0.45%
Stevens, 1999[54]	LOCM, HOCM (decision was made by operating physician)	IA	Not specified	1	IVF alone	IV	150ml/h of 0.45 NS before and during procedure then 6h after followed by hourly adjustment to match prior hour's urine output, before procedure, during procedure, and for at least 6 hrs after the procedure	Randomized to control or experimental arm, then the decision re: mannitol depended on the pulmonary capillary wedge pressure. All arms given 0.45 saline
				2	IVF + furosemide + dopamine + mannitol	IV	Furosemide 1mg/kg to max of 100mg single dose+ dopamine 3mcg/kg/min upon arrival to the catheterization lab and continued during the procedure + mannitol 12.5g in 250ml 5%dextrose (if PCWP < 20)+ control arm treatment, Before, during and at least 6 hrs after procedure	
				3	IVF + furosemide + dopamine	IV	Furosemide 1mg/kg to max of 100mg single dose+ dopamine 3mcg/kg/min upon arrival to the catheterization lab and during procedure (no mannitol if PCWP was at least 20)+ control arm treatment, Before, during and at least 6 hrs after procedure	

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Talati, 2012 [55]	Iodixanol	NR	Not specified	1	No fenoldapam	NR	NR, NR, Not stated	All participants received hydration, not specified
				2	Fenoldopam	Other, intrarenal	Range: 0.1 - 0.4 ug/kg per min, Mean: 46.5 (SD: 5.5) min, Not stated,	
Tamura, 2009 [55]	Iohexol	IA	Not specified	1	Normal Saline	IV	Standard hydration with sodium chloride was intravenous administration with isotonic saline (0.9%) at a rate of 1 ml/kg/hour (0.5 ml/kg/hour for patients with left ventricular ejection fraction < 40%) for 12 hours before and 12 hours after an elective coronary procedure. For patients weighing >80 kg, infusion rate was limited to 80 ml/hour (40 ml/hour for patients with left ventricular ejection fraction < 40%).	
				2	Normal Salinde + Bicarbonate	IV	Standard hydration with sodium chloride was intravenous administration with isotonic saline (0.9%) at a rate of 1 ml/kg/hour (0.5 ml/kg/hour for patients with left ventricular ejection fraction <40%) for 12 hours before and 12 hours after an elective coronary procedure. For patients weighing >80 kg, infusion rate was limited to 80 ml/hour (40 ml/hour for patients with left ventricular ejection fraction <40%).	
Thiele, 2010[68]	Iopromide	IA	Not specified, Define, median=180 ml	1	Placebo	IV	10ml of nacl 0.9% before angio, 10 mls twice daily for 48h after PCI, 48 hours, Prior to CM administration After CM administration	After PCI, all treated and control patients underwent hydration with intravenous nacl (0.9%) infusion at a rate of 1ml/kg of body weight per h for 12 h (or 0.5ml/kg/h in overt heart failure)
				2	Nac	IV	1,200mg twice daily, 6000mg, 48 hours, Prior to CM administration After CM administration	IV bolus of 1,200 mg before angioplasty and 1,200 mg intravenously twice daily for the 48 h after PCI (total dose 6,000 mg
Trivedi,2003 [56]	LOCM	IA	Dose and duration not specified. Mean Volume: Arm 1 mean=187.3 ml; Arm 2 mean=201.3	1	Oral hydration	Oral	Unrestricted fluids, Not stated	After catheterization, all subjects were routinely encouraged to partake oral fluids.

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
Trivedi,2003 [56] (continued)				2	Iv hydration(0.9% saline	IV	0.9% saline for 24 h at a rate of 1 ml/kg/h beginning 12 h prior to scheduled catheterization, 24h, Prior to CM administration During CM administration After CM administration	After catheterization, all subjects were routinely encouraged to partake oral fluids.
Weisberg, 1994 [57]	Other description, MD76 (66% diatrizoate meglumine, 10% diatrizoate sodium); it is an ionic, high-osmolality medium	IA	Not specified	1	Saline	IV	Saline 0.45% 100ml/h, 2h (not counting > 12 hrs of hydration pre-procedure; see below), During CM administration After CM administration Other, as below, all patients received IVF starting 12 hours pre-procedure	All patients received IV infusion of 0.45% nacl at 100 cc/hr beginning 12 hours before, and continuing throughout cardiac catheterization. Patients were randomly assigned to receive either saline or one of 3 drugs by IV infusion. The unfusions began immediately after full instrumentation for cardiac catheterization and continued for a total of two hours (~ 2x the duration of the procedure).
				2	Dopamine	IV	Dopamine 2ug/kg/min in 0.45% NS at 100 ml/hr, 2h, During CM administration After CM administration Other, as below, all patients received IVF starting 12 hours pre-procedure	All patients received IV infusion of 0.45% nacl at 100 ml/hr beginning 12 hours before, and continuing through the cardiac catheterization
				3	Anp	IV	ANP 50ug bolus then infusion 1ug/min in 0.45% nacl at 100 ml/hr, 2h, During CM administration After CM administration Other, as below, all patients received IVF starting 12 hours pre-procedure	All patients received IV infusion of 0.45% nacl at 100 ml/hr beginning 12 hours before, and continuing through the cardiac catheterization
				4	Mannitol	IV	Mannitol 15g/dl in 0.45 nacl at 100 ml/hr, 2h, During CM administration After CM administration Other, as below, all patients received IVF starting 12 hours pre-procedure	All patients received IV infusion of 0.45% nacl at 100 ml/hr beginning 12 hours before, and continuing through the cardiac catheterization

Evidence Table C. Interventions for studies comparing interventions to prevent development of CIN (continued).

Author, year	Contrast Medium	Contrast Administration	Dose, Duration, Volume	Arm	Intervention	Administration	Intervention: dose, duration temporal association to contrast	Other intervention details
XinWei, 2009[58]	Iodixanol, Iohexol	IA	Body weight (kg) x 5ml/serum creatinine.	1	Simvastatin 20	Oral	20mg/day from admission to the day before PCI, and then resumed simvastatin 20 mg/day for the following days, Up to 48hrs after procedure. Prior and After CM administration	All patients were hydrated with intravenous isotonic saline (0.9%) at a rate of 1 ml/kg body weight per hour for 6 to 12 hours before and 12 hours after coronary catheterization to achieve a urinary flow rate of
				2	Simvastatin 80	Oral	80mg/day from admission to the day before PCI, and then resumed simvastatin 20 mg/day for the following days. Up to 48hrs after procedure. Prior and After CM administration	
Yin, 2013 [59]	Other description, Ultravist-nonionic, low-osmolality contrast medium	IA	Not specified, Not specified	1	No probucol	IV	.9% isotonic saline(1ml/kg/hr), 24 hours, After CM administration	After coronary intervention, all patients underwent hydration with intravenous isotonic saline (0.9%) at a rate of 1 ml per kilogram of body weight per hour (or 0.5 ml per kilogram After coronary intervention, all patients underwent hydration with intravenous isotonic saline (0.9%) at a rate of 1 ml per kilogram of body weight per hour (or 0.5 ml per kilogram per hour in the cases of overt heart failure) for 24 h.
				2	Probucol	Oral, IV	1000mg before procedure and 500mg twice daily after, before procedure and 3 days after procedure, Prior to CM administration After CM administration	After coronary intervention, all patients underwent hydration with intravenous isotonic saline (0.9%) at a rate of 1 ml per kilogram of body weight per hour (or 0.5 ml per kilogram

ACEI= Angiotensin Converting Enzyme Inhibitor, ANP=Atrial Natriuretic Peptide, AVH= Amlodipine Valsartan Hydration, b.i.d=Bi-daily, Bev=Beverage, CAG=Coronary Angiogram, Cc/hr= cubic centimeter per kilogram, CECT=Contrast Enhanced Computed Tomography, CM=Contrast Media, H=Hour, HD=Hemodialysis, hrs=hours, IA=Intrarterial, IOCM=Iso-Osmolar Contrast Media, IQR=Interquartile Range, IV=Intravenous, IVF=Intrvenous Fluid, LCA=Left Coronary Artery, LOCM=Low-Osmolar Contrast Media, Mcg/kg/min=microgram per kilogram per min, MD= Doctor of Medicine, mEq/l= milliequivalents per liter, Mg/dl=milligram per deciliter, Mg/kg/hour=milligram per kilogram per hour, Mg/kg=milligram per kilogram, Mg=milligram, mls=milliliters, mOsm/kg= milliosmoles per kilogram, N/A=Not Applicable, NAC=N-acetylcysteine, NaCl=Sodium Chloride, NaHCO3=Sodium Bicarbonate, NR=Not Reported, Osm=Omsolarity, p.o.=By Mouth, PCI=Percutaneous Coronary Intervention, PCWP=Pulmonary Capillary Wedge Pressure, POBID=By mouth twice daily, RCA=Right Coronary Artery, SB=Sodium Bicarbonate, SD=Standard Deviation, Ug/kg/min=microgram per kilogram per minute, VO=Vocal Order

Evidence Table D. Summary of studies of N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	Number randomized (Number analyzed if differerent)	Population	Age, years (or range of means[¶])	No. female (%)[§]	Total follow-up	CM Route*	Definition of CIN*	Study limitations†
Allaqaband, 2002 [5]	IV 0.45% saline vs. oral NAC + IV 0.45% saline vs. IV IV fenoldopam + 0.45% saline +	126 (123)	CKD (SrCr ≥ 1.6 mg/dl or an estimated creatinine clearance ≤ 60 ml/min)	71	52 (42)	48 hours	LOCM IA	A2a	M
Baskurt, 2009[8]	IV normal saline vs. oral NAC + IV normal saline vs. Oral NAC + oral theophylline + IV normal saline	217	Moderate degree (stage 3) CKD (eGFR between 30 and 60 ml/min/1.73 m^2)	67	87 (40)	12 months	LOCM (Ioversol) IA	A2b	H
Briguori, 2004 [9]	Oral NAC + IV 0.45% saline vs. IV fenoldopam + IV 0.45% saline	192	CKD (stable SrCr ≥ 1.5 mg/dl and/or creatinine clearance < 60 mL/min)	68-69	29 (15)	48 hours	IOCM (Iodixanol), IA	A2b	M
Briguori, 2004[10]	Oral NAC single-dose (600 mg bid) + IV 0.45% saline vs.Oral NAC double-dose (1200 mg bid) + IV 0.45% saline	223	CKD (stable SrCr ≥table SrCr ed/or creatinine clearance <60 ml/min)	66-67	41 (18)	48 hours	Iobitriol IA	A2b	M
Briguori, 2007[11]	Oral NAC + IV normal saline vs. Oral NAC + IV NaHCO3 in dextrose and water vs Oral NAC + IV ascorbic acid + IV normal saline	351 (326)	CKD (SrCr ≥2.0 mg/dl and/or estimated GFR < 40 ml/min/1.72m^2	69-71	57 (17)	48 hours	Iodixanol IA	A1b	M
Brueck, 2013 [69]	IV normal saline + placebo vs. IV NAC + IV normal saline vs. IV ascorbic acid + IV normal saline	520 (499)	SrCr ≥ 1.3 mg/dl	74-75	181 (36)	72 hours	Iopromide (LOCM) IA	A2b	L
Castini, 2010[70]	IV normal saline vs. + IV normal salinevs. IV NaHCO3	156	SrCr ≥ 1.2 mg/dl	70-72	19 (12)	5 days	Iodixanol (IOCM) IA	A1b	M
Chen, 2008 [13]	If SrCr <1.5 mg/dL:No intravenous fluids vs. IV 0.45% saline. If SrCr ≥1.5 mg/dL, then NAC + IV 0.45% saline vs. NAC without intravenous fluids	936	Myocardial Ischemia, scheduled for percutaneous coronary intervention (PCI)	56-67	84	6 months	IOCM IA	A2a	H
Demir, 2008 [15]	IV normal saline vs. NAC + IV normal saline vs. misoprostol + IV normal saline + vs. theophylline+ IV normal saline vs. nifedipine + + normal saline	97	Non-diabetic, no CKD	43-78	43 (44)	72 hours	Iomeprol, Iopamidol IV	A3b	H
Gunebakmaz, 2012[20]	normal saline vs. normal saline + nebivolol vs. NAC + normal saline	120	SrCr ≥ 1.2 mg/dl	64-66	38 (31)	5 days	Iopromide IA	A3b	H

Evidence Table D. Summary of studies N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	N	Population	Age, range of means¶	No. female (%)§	Total follow-up	CM Route*	Definition of CIN*	Study limitations†
Hafiz, 2012 [21]	IV normal saline with or without oral NAC vs. IV NaHCO3 in 5% dextrose in water with or without oral NAC	320	SrCr >1.6 mg/dl in non-diabetics and >1.4 mg/dl in diabetics or an estimated glomerular filtration rate (eGFR) of <50 ml/min/1.73 m^2	73	138 (43)	48 hours	LOCM IA	A3a	M
Heguilen, 2013 [24]	IV NaHCO3 vs. NAC + IV NaHCO3 vs. NAC + IV normal saline	133 (123)	Stable SrCr ≥1.25 mg/dl or estimated creatinine clearance > 45 ml/min, but SrCr must be ≤ 4.5 mg/dl	64-69	34 (25)	72 hours	Ioversal IA	A1b	M
Holscher, 2008[25]	IV normal saline + glucose vs. + hemodialysis IV normal saline +glucose vs. oral NAC + IV normal saline + g glucose	412	SrCr 1.3-3.5 mg/dl	67	68 (16.5)	30 days	Iopromide IA	A2b	H
Huber, 2006[26]	IV ttheophylline vs. IV NAC vs. IV theophylline + IV NAC	91	At least one risk factor for CIN; stable renal function	58.5	31 (34)	48 hours	Iomeprol (LOCM) IA and IV	See footnote ‡	M
Kinbara, 2010[28]	IV normal saline vs. + IV aminophylline + normal saline vs. NAC + normal saline	45	Stable coronary artery disease and stable SrCr	70-71	17 (37)	48 hours	Iopamidol IA	A2a	M
Kotlyar, 2005[32]	IV normal saline vs IV NAC 300mg in 5% dextrose + IV normal saline + vs. IV NAC 600mg in 5% dextrose + IV normal saline	65 (60)	Stable SrCr concentrations ≥0.13 mmol/l (1.47 mg/dl)	66-69	7 (11)	30 days	Iopromide IA	A2b	M
Marenzi, 2006 [40]	IV normal saline + placebovs. standard-dose NAC (600 mg IV NAC before the procedure, then 600 mg twice a day for 48 hrs after the contrast) + normal saline vs. High-dose NAC + (1200 mg IV NAC before the contrast, then 1200 mg orally twice a day for 48 hours after) + IV normal saline	354	ST eleveation acute myocardial infarction	62-62	50 (14)	NR	Iohexol IA	A1b	M
Ng, 2006 [44]	Oral NAC + IV normal saline vs. IV fenoldopam + IV normal saline	95 (84)	Stable renal disease, SrCr >1.2 mg/dl	68	24 (25)	72 hours	Only non-ionic LCOM or IOCM IA	A3a	M
Ozcan, 2007[71]	IV normal saline vs NAC + IV normal saline vs IV NaHCO3 in dextrose	264	SrCr > 1.2 mg/dl and ≤ 4 mg/dl	69	67 (25)	48 hours	Ioxaglate (LOCM) IA	A3a	H
Ozhan, 2010[46]	NAC + IV saline vs. NAC + atorvastatin + IV saline	130	No renal insufficiency (SrCr ≤ 1.5 and GFR ≥ 70 ml/min)	54-55	53 (41)	48 hours	Iopamidol IA	A3a	M

Evidence Table D. Summary of studies N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	N	Population	Age, range of means¶	No. female (%)§	Total follow-up	CM Route*	Definition of CIN*	Study limitations†
Ratcliffe, 2009 [48]	IV normal saline in 5% dextrose vs. NAC + IV normal saline in 5% dextrose vs. IV NaHCO3 in 5% dextrose vs. NAC + IV NaHCO3 in 5% dextrose	118 (78)	CKD and/or diabetes mellitus	66	31(40)	7 days	Iodixanol (IOCM) IA	A1a	H
Recio-Mayoral, 2007 [49]	Oral NAC post-contrast + IV normal saline vs. IV NAC pre- contrast oral NAC post-contrast+ IV sodium bicarbonate in 5% glucose and water	111	Patients with myocardial infarction treated with PCI or high-risk non-ST segment elevation acute coronary syndrome needing urgent revascularization (no GFR inclusion criteria other than the exclusion of dialysis patients)	65	34 (31)	7 days	Iomeprol (LOCM) IA	A2b	H
Reinecke, 2007 [50]	IV normal saline +5% glucose vs. one session of hemodialysis + IV normal saline + 5% glucose vs. oral NAC + IV normal saline + 5% glucose	424 (412)	SrCr 1.3-3.5 mg/dl	67-68	73 (17)	Mean follow-up: 553 days (63 to 1316 days)	Iopromide (IOCM) IA	A2b	H

%=percent; CIN=contrast induced nephropathy; CKD=chronic kidney disease; CM=contrast media; dL=deciliter; eGFR=estimated glomerular filtration rate; IA=intrarterial; IV=intravenous; LOCM=low-osmolar contrast media; m^2=meter squared; mg=milligram; min=minute; ml=milliliter; mmol/l=millimole per liter; N=sample size; NAC=N-acetylcysteine; NaHCO3=sodium bicarbonate; NR=not reported; PCI=percutaneous coronary intervention; SrCr=serum creatinine

* CIN definitions: rise in serum creatinine relative to baseline: >25% (A1a); ≥25% (A1b); >0.5 mg/dl (A2a); ≥0.5 mg/dl (A2b); >25% or > 0.5 mg/dl (A3a); ≥25% or ≥0.5 mg/dl (A3b); ≥50% (A4) B: >25% reduction in creatinine clearance

† Study limitations: L=low risk of bias; M=medium risk of bias; H=high risk of bias

‡Barrett BJ, Parfrey PS. Prevention of nephrotoxicity induced by radiocontrast agents, N Engl J Med 1994;331:1449–1450.

§ Percent females in entire study population

¶ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms if the mean age for the whole population is not reported

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Allaqaband, 2002 [5]	Arm1: IV 0.45% saline Arm2: NAC + IV 0.45% saline + Arm3: IV fenoldopam IV 0.45% saline +	Cr >0.5 mg/dl at 48 hours Arm1: 6/40 (15.3) Arm2: 8/45 (17.7) Arm3: 6/38 (15.7); P=0.919	Diabetics Cr >0.5 mg/dl at 48 hours Arm1: 3/6 (50) Arm2: 5/8 (62.5) Arm3: 4/6 (66.6); P=0.803 Use of Calcium channel antagonists Cr >0.5 mg/dl at 48 hours Arm1: 5/6 (83.3) Arm2: 3/8 (37.5) Arm3: 2/6 (33.3); P=0.150 Use of ACE inhibitors Cr >0.5 mg/dl at 48 hours Arm1: 3/6 (50) Arm2: 4/8 (50) Arm3: 2/6 (33.3); P=0.857	NR	Time point: NR 2 (1.62% of all participants)	At 24 hours: Arm1: 0.09 (0.21) Arm2: 0.08 (0.37) Arm3: 0.13 (0.25); P=0.785 At 48 hours: Arm1: 0.09 (0.30) Arm2: 0.01 (0.62) Arm3: 0.01 (0.37); P=0.701	NR	Three participants in Arm 3 were withdrawn because of hypotension. Other cardiac events NR.
Baskurt, 2009[8]	Arm1: IV normal saline Arm2: Oral NAC + IV normal saline Arm3: Oral NAC + oral theophylline + IV normal saline	Cr ≥0.5 mg/dl at 48 hours Arm1: -5/72 (6.9) Arm2: 7/73 (9.6) Arm3: 0/72 (0); P=0.033	NR	No deaths were were observed in the 1-year follow-up of the participants who had developed CIN	0 (0%)	NR	NR	No major adverse cardiac events were observed in the 1-year follow-up of the participants who had developed CIN

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in SrCr, mean (SD) or Baseline and Follow-up SrCr	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Briguori, 2004 [9]	Arm 2: oral NAC + IV 0.45% saline Arm3 IV fenoldopam + IV 0.45% saline	SrCr ≥0.5 mg/dl at 48 hours Arm2: 4/97 (4.1) Arm3: 13/95 (13.7) OR 0.27 (95% CI: 0.08-0.85) P=0.019	Baseline SrCr > 2.5 mg/dL SrCr ≥0.5 mg/dl at 48 hours Arm2: 1/9 (11.0) Arm3: 5/11 (45.5); P=0.095 Diabetes SrCr ≥0.5 mg/dl at 48 hours Arm2: 3/49 (6.1) Arm3: 4/49 (8.2); P=0.72 LVEF <40% SrCr ≥0.5 mg/dl at 48 hours Arm2: 0/10 (0) Arm3: 4/13 (13.3); P=0.23 LVEF ≥40% SrCr ≥0.5 mg/dl at 48 hours Arm2: 4/87 (4.5) Arm3: 9/72 (12.5); P=0.085 Diabetes and LVEF < 40% SrCr ≥0.5 mg/dl at 48 hours Arm1: 0/9 (0) Arm2: 0/7 (0)	One of 95 (1.0%) participants in Arm 3 experienced in-hospital death.	At 48 hours Arm2: 0/97 (0) Arm3: 1/95 (1.1); P=NR	Arm2: Median (IQR): Baseline: 1.72 mg/dL (1.55 to 1.90) 48 hours: 1.60 (1.40 to 1.86) Arm3: Median (IQR): Baseline: 1.75 mg/dL (1.62 to 2.01) 48 hours: 1.71 (1.48 to 2.03) P = 0.17 between baseline values, P=0.77 between 48-hour values	Arm2: 2.9 (2.7) Arm3: 5.0 (10); P=0.049	Two of 95 participants (2.1%) in Arm 3 had severe hypotension.

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in SrCr, mean (SD) or Baseline and Follow-up SrCr	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Briguori, 2004[10]	Arm2: Oral NAC single-dose (600 mg bid) + IV 0.45% saline Arm3: Oral NAC double-dose (1200 mg bid) + IV 0.45% saline	Cr ≥0.5 mg/dl at 48 hours or need for dialysis Arm2: 12/109 (11) Arm3: 4/114 (3.5) OR 0.29 (95% CI: 0.09-0.94) P=0.038	Diabetics Renal function deterioration occurred in: Arm2: 4/47 (2.1) Arm3: 1/47 (2.1); P = 0.36 Left ventricular ejection fraction < 40% Renal function deterioration occurred in: Arm2: 4/22 (18.2) Arm3: 1/16 (6.3); P=0.37	NR (No apparent deaths because all participants had lab drawn at 48 hours)	0 (0)	Arm2: Median (IQR) Baseline: 1.56 (1.47 to 1.71) 48 hours: 1.50 (1.33 to 1.69) Arm3: Median (IQR) Baseline: 1.61 (1.45 to 1.86) 48 hours: 1.46 (1.31 to 1.83) P=0.14 between baseline values P=0.77 between 48-hour values	Length of hospitalization Arm2: 2.6 (0.9) Arm3: 2.2 (0.6); P=0.018	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Briguori, 2007[11]	Arm2: Oral NAC + IV normal saline Arm3: Oral NAC + IV NaHCO3 in dextrose and water Arm4: Oral NAC + IV ascorbic acid + IV normal saline	Increase in SrCr ≥25% at 48 hours Arm2: 11/111 (9.9) Arm3: 2/108 (1.9) Arm4: 11/107 (10.3); P=0.010 Cr ≥0.5 mg/dl At 48 hours Arm2: 12/111 (10.8) Arm3: 1/108 (0.9) Arm4: 12/107 (11.2); P=0.026	Odds Ratio (95% CI) compared to Arm2: Diabetics Arm3: 0.6 (0.42-0.86) Arm4: 1.73 (0.59-5.10) No diabetes Arm3: 0.45 (0.36-0.56) Arm4: 0.21 (0.02-1.86) Other subgroups are reported in Figure 3	NR It is inferred that there were no death (all participants are accounted for)	Arm2: 1 (0.9) Arm3: 1 (0.9) Arm4: 4 (3.8); P=NR	Arm2: Median (IQR) Baseline: 1.95 (1.69 to 2.26) 48 hours: 1.88 (1.54 to 2.36) Arm3: Median (IQR) Baseline: 2.04 (1.88 to 2.36) 48 hours: 1.90 (1.67 to 2.29) Arm4 Median (IQR): Baseline: 1.93 (1.82 to 2.16) 48 hours:1.88 (1.53 to 2.32) P=0.14 between baseline values P=0.77 between 48-hour values	NR	NR

Brueck, 2013[69]	Arm1: IV normal saline + placebo Arm2: IV NAC + IV normal saline Arm3: IV ascorbic acid + IV normal saline	Increase in SrCr ≥0.5 mg/dL at 72 hours Arm1: 62/193 (32.1) Arm2: 53/192 (27.6) Arm3: 24/98 (24.5); Arm1 vs Arm2: P=0.20 Arm1 vs Arm3: P=0.11	Diabetes Cr ≥0.5 mg/dL at 72 hours: Arm1: 36/102 (35.0) Arm2: 24/86 (28.4) Arm3: 14/48 (29.8) Arm1 vs. Arm2: P=0.65Arm1 vs. Arm3: P=0.62 SrCr ≤ 1.4 at baseline CIN at 72 hours: Arm1: 33.7% Arm3: 10.6%; P =0.0048 SrCr > 1.4 mg/dL at baseline CIN at 72 hours: Arm1: 30.9% Arm3: 37.3%; P = 0.14	NR	0(0)	At 72 hours Arm1: 0.2 (0.35). IQR 0.2 (0-0.5) mg/dL Arm2: 0.15 (0.31), IQR 0.1 (0-0.2) mg/dL Arm3: 0.17 (0.37); IQR 0.2 (0-0.2) mg/dL. P<0.001	NR	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Castini, 2010[70]	Arm1: IV normal saline Arm2: NAC + IV normal saline +Arm3: IV NaHCO3	Increase in SrCr ≥25% within 5 days, but author provided data a 48 hours (personal communication): At 48 hours: Arm1: 4/51 (8) Arm2: 8/53 (17) Arm3: 5/52 (14); P=NR At 5 days: Arm1: 7/51 (14) Arm2: 9/53 (17) Arm3: 7/52 (14); P=0.85 Increase in SrCr ≥0.5 mg/dl : 48 hours Arm1: 4/51 (8) Arm2: 5/53 (9) Arm3: 4/52 (8); P=NR At 5 days: Arm1: 4/51 (8) Arm2: 5/53 (9) Arm3: 6/52 (12); P=0.82	NR	NR	0(0)	At 24 hours Arm1: 1.37 (0.33) Arm2: 1.49 (0.40) Arm3: 1.53 (NR); P=NS At 48 hours Arm1: 1.50 (NR) Arm2: 1.59 (NR) Arm3: 1.69 (0.50); P=NS At 5 days Arm1: 1.47 (NR) Arm2: 1.56 (NR) Arm3: 1.56 (NR); P=NR	NR	NR

Chen, 2008 [13]	If Sr Cr < 1.5 mg/dl Arm1: NoIV fluids Arm2: IV 0.45% saline If SrCr ≥ 1.5 mg/dl: Arm3: Oral NAC without IV fluids Arm4: Oral NAC + IV 0.45% saline	Increase in SrCr >0.5 mg/dl at 48 hours Arm1: 23/330 (6.97) Arm2: 22/330 (6.67) Arm3: 64/188 (34.04) Arm4: 40 (21.28); P<0.001 Arm1 vs. Arm2 P>0.05 Arm3 vs. Arm4 P<0.01	NR	Death rates were reported by creatinine groups, but were not categorized by treatment arm.	The incidence of continuous veno-venous hemofiltration initiation was reported by creatinine group, but was not categorized by treatment arm.	NR	NR	The overall incidence of arrhythmias and stroke were reported by creatinine group, but not be treatment arm.

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Demir, 2008 [15]	Arm1: IV normal saline Arm2: NAC + IV normal saline Arm3: Misoprostol + IV normal saline Arm4: Theophylline + IV normal saline Arm5:Nnifedipine +IV normal saline	Increase in SrCr ≥25% or ≥0.5 mg/dl within 72 hours Arm1: 0/20 (0) Arm2: 1/20 (5) Arm3: 0/20 (0) Arm4: 4/20 (20) Arm5: 0/17 (0); P=NR	NR	NR	NR	NR	NR	NR
Gunebakmaz, 2012[20]	Arm1: IV normal saline Arm2: Nebivolol + IV normal saline Arm3: NAC + IV normal saline	Increase in SrCr ≥25% and/or or ≥0.5 mg/dl at 72 hours Arm1: 11/40 (27.5) Arm2: 8/40 (20.0) Arm3: 9/40 (22.5); P=0.72	NR	NR	NR	NR	NR	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Hafiz, 2012 [21]	Arm1: IV normal saline with or without oral NAC Arm2: IV NaHCO3 in 5% dextrose in water without or without oral NAC	Increase in SrCr >25% or >0.5 mg/dl at 48 hours Arm1: 19/161 (11.8) Arm2: 14/159 (8.8); P=>0.05	without NAC Cr >25% or >0.5 mg/dl at 48 hours Arm1: 11/80 (13.8) Arm2: 6/79 (7.6); P=>0.05 without NAC Cr >25% or >0.5 mg/dl at 48 hours Arm1: 8/81 (9.9) Arm2: 8/80 (10.0); P=>0.05 Age (increasing years) Cr >25% or >0.5 mg/dl at 48 hours OR: 1.05 (95% CI: 1.02-1.08); P=0.001 Gender (female) Cr >25% or >0.5 mg/dl at 48 hours OR: 0.49 (95% CI: 0.21-1.13); P=0.095 OR: 3.42 (95% CI: 1.46-7.98); P=0.005 ACE inhibitors Cr >25% or >0.5 mg/dl at 48 hours OR: 0.1.12 (95% CI: 0.51-2.50); P=0.775	At 48 hours Arm1: 0/161 (0) Arm2: 0/159 (0); P=NR	NR	NR	NR	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Hafiz, 2012 [21] (continued)			Higher baseline Cr level Cr >25% or >0.5 mg/dl at 48 hours OR: 0.64 (95% CI: 0.35-1.19); P=0.161 Diabetes Cr >25% or >0.5 mg/dl at 48 hours OR: 1.57 (95% CI: 0.69-3.35); P=0.281 Contrast volume >3ml/kg Cr >25% or >0.5 mg/dl at 48 hours OR: 1.10 (95% CI: 1.00-1.20); P=0.038 GFR SrCr >25% or >0.5 mg/dl at 48 hours OR: 0.99 (95% CI: 0.98-1.01); P=0.435 Anemia Cr >25% or >0.5 mg/dl at 48 hours OR: 1.97 (95% CI: 0.42-9.29); P=0.390 Diuretics Cr >25% or >0.5 mg/dl at 48 hours OR: 3.42 (95% CI: 1.46-7.98); P=0.005					

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Heguilen, 2013 [24]	Arm1: IV NaHCO3 Arm2: NAC + IV NaHCO3 Arm3: NAC + IV normal saline	Increase in SrCr ≥ 25% at 72 hours Arm1: 15/42 (35.7) Arm2: 3/43 (6.98) Arm3: 6/38 (15.8); P<0.01	Acute myocardial infarction Cr ≥25% at 72 hours OR: 0.36 (95% CI: 0.08-1.54); P=0.17 Hypertension Cr ≥25% at 72 hours OR: 2.31 (95% CI: 0.40-13.31); P=0.35 Left ventricular dysfunction Cr ≥25% at 72 hours OR: 0.66 (95% CI: 0.12-3.53); P=0.63 NAC use Cr ≥25% at 72 hours OR: 0.18 (95% CI: 0.04-0.72); P=0.016 Contrast volume Cr ≥25% at 72 hours OR: 0.10 (95% CI: 0.99-1.02); P=0.10	NR	NR	At 2-3 days Arm1: 1.74 (0.09) Arm2: 1.44 (0.06) Arm3: 1.69 (0.16); P=NR	NR	NR
Holscher, 2008[25]	Arm1: IV normal saline with 5% glucose Arm2: IV normal saline with 5% glucose +hemodialysis Arm3: Oral NAC + IV normal saline with 5% glucose	Increase in SrCr ≥0.5 mg/dl at 72 hours Arm1: 10/139 (7.2) Arm2: 22/134 (16.4) Arm3:6/139 (4.3) P=0.68	NR	NR by arm, but there were 73 deaths overall within the follow-up period	NR	NR	NR	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Huber, 2006[26]	Arm1: theophylline Arm2: NAC Arm3: theophylline + NAC	Based on prior definition (see summary table) at 48 hours Arm1: 1/51 (2) Arm2: 6/50 (12) Arm3: 2/49 (4); P=<0.001 Arm1 vs. Arm2 P=0.47 Arm2 vs. Arm3 p=0.146 Arm1 vs. Arm3 p=0.53	SrCr > 1.5 mg/dl Arm1: 0/12 (0) Arm2: 5/11 (45) Arm3: 1/14 (7) Arm1 vs Arm3: P=0.345	At 12 days Arm1: 3/51 (5.9) Arm2: 1/50 (2.0) Arm3: 0/49 (0); P=NR	1 patient required dialysis, no other details	NR	NR	NR
Kinbara, 2010[28]	Arm1: IV normal saline Arm2: IV aminophylline + normal saline Arm3: NAC + IV normal saline	Increase in SrCr >0.5 mg/dl at 48 hours Arm1: 4/15 (26.7) Arm2: 0/15 (0) Arm3: 0/15 (0); P=0.0109	NR	NR	NR	At 48 hours Arm1: 0.95 (0.21) to 1.28 mg/dl (0.21), P<0.01 Arm2: 0.97 (0.29) mg/dl at baseline; unchanged at 48 hours Arm31.00 (0.36) mg/dl to 0.67 (0.16), P<0.01	NR	NR
Kotlyar, 2005[32]	Arm1: normal saline Arm2: NAC 300mg + normal saline + dextrose Arm3: NAC 600mg + normal saline + dextrose	Increase in SrCr ≥ 0.044 mmol/l (≥ 0.5 mg/dl at 48 hours Arm1: 0/19 (0) Arm2: 0/20 (0) Arm3: 0/21 (0); P=NR	NR	One patient died during the catheterization (not related to study protocol)	Chronic reduction in renal function at 30 days Arm1: 2/19 (11) Arm2: 4/20 (20) Arm3: 2/21 (10); P=0.66	NR	NR	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Marenzi, 2006 [40]	Arm1: placebo + IV normal saline Arm2: standard-dose NAC+ IV normal saline Arm3: high-dose NAC+ IV normal saline	Increase in SrCr ≥ 25% at 72 hours Arm1: 39/119 (33) Arm2: 17/115 (15) Arm3: 10/118 (8); P=<0.001 Increase in SrCr ≥0.5 mg/dl at 72 hours Arm1: 22/119 (18) Arm2: 7/115 (6) Arm3: 4/118 (3); P=<0.001	CrCl ≤60 ml/min Cr >25% at 72 hours Arm1: (43) Arm2: (27) Arm3: (19); P=0.25 CrCl>60 ml/min Cr >25% at 72 hours Arm1: (29) Arm2: (10) Arm3: (5); P=0.25 LVEF ≤40% Cr >25% at 72 hours Arm1: (63) Arm2: (33) Arm3: (23); P=0.71 LVEF >40% Cr >25% at 72 hours Arm1: (24) Arm2: (11) Arm3: (5); P=0.71	Time point NR Arm1: 13/119 (11) Arm2: 5/115 (4) Arm3: 3/118 (3); P=0.007	Time point NR Arm1: 6/119 (5) Arm2: 2/115 (2) Arm3: 1/118 (1); P=0.14	NR	NR	Cardiogenic shock Arm1: 12/119 (10) Arm2: 6/115 (5) Arm3: 8/118 (7); P=0.35 High-rate atrial fibrillation Arm1: 10/119 (8) Arm2: 4/115 (3) Arm3: 10/118 (8); P=0.,22 Cardiopulmonary resuscitation, ventricular tachycardia, or ventricular fibrillation Arm1:17/119 (14) Arm2: 12/115 (10) Arm3: 8/118 (7); P=0.17 High-degree conduction disturbances Arm1: 10/119 (8) Arm2: 6/115 (5) Arm3: 8/118 (7); P=0.63 Acute pulmonary edema requiring mechanical ventilation Arm1: 9/119 (8) Arm2: 2/115 (2) Arm3: 2/118 (22); P=0.03

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Ng, 2006 [44]	Arm1: Oral NAC + IV normal saline Arm2: IV fenoldopam + IV normal saline	Increase in SrCr >25% or ≥ 0.5 mg/dl at 72 hours Arm1: 5/44 (11.4) Arm2: 8/40 (20.0); P=0.4	At 72 hours: There were no differences in the incidence of CIN in the subgroups that were analyzed (diabetics vs non-diabetics, SrCr > 1.7 and 2 mg/dL, gender, age > 70 years, and contrast volume of at least 150 and 200 mL.)	NR	NR	At 72 hours Arm1: 0.20 (0.72) Arm2: 0.08 (0.48); P=0.4 Diabetics at 72 hours Arm1: 0.44 (1.12) Arm2: 0.23 (0.65); P=0.5 Non-diabetics at 72 hours Arm1: 0.04 (0.17) Arm2: -0,01 (0.34); P =0.3	NR	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Ozcan, 2007[71]	Arm1: IV normal saline Arm2: NAC + IV normal saline Arm2: IV NaHCO3 in dextrose Arm3:	Increase in SrCr >25 or 0.5 mg/dL at 48 hours Arm1: 12/88 (13.6) Arm2: 11/88 (12.5) Arm3: 4/88 (4.5) Arm1 vs. Arm2: RR 0.95 (95% CI: 0.37-2.17) P=0.82 Arm1 vs. Arm3: RR 0.30 (95% CI: 0.09-0.97) P=0.036 Arm2 vs. Arm3: RR 0.33 (95% CI: 0.10-1.09) P=0.059	NR	NR	At 48 hours Arm1: 1/88 (1.14) Arm2: 0/88 (0) Arm3: 1/88 (1.14); P=NR	At 48 hours Arm1: 0.02 Arm2: 0.01 Arm3: -0.01; P=0.04	NR	Congestive heart failure at 48 hours Arm1: 0/88 (0) Arm2: 0/88 (0) Arm3: 0/88 (0); P=NR
Ozhan, 2010[46]	Arm2: NAC + IV saline Arm3: NAC + atorvastatin+ IV saline	Increase in SrCr >25% or >0.5 mg/dl at 48 hours Arm1: 7/70 (10) Arm2: 2/60 (3.33); P=0.135	NR	NR	NR	At 48 hours: Arm2: 0.06 (0.25) Arm3: -0.02 (0.13); P=0.023	NR	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Ratcliffe, 2009 [48]	Arm1: IV normal saline in 5% dextrose Arm2: NAC + IV normal saline in 5% dextrose Arm3: IV NaHCO3 in 5% dextrose Arm4: NAC + IV NaHCO3 in 5% dextrose	SrCr >25% at 72 hours Arm1: 1/15 (7) Arm2: 1/21 (5) Arm3: 2/19 (11) Arm4: 1/23 (4); P=0.863	There were no significant differences between the sugroups (renal insufficiency and/or diabetes mellitus) in CIN incidence; P=0.313	NR	NR	Change in SrCr (micromol/L*): At 72 hours Arm1: 6.19 (30.06) Arm2: 7.07 (13.26) Arm3: 7.96 (15.03 Arm4: -1.77 (14.14); P=0.287 Maximum change in SrCr (micromol/L*): Arm1: 10.6 (29.17) Arm2: 9.72 (13.26) Arm3: 14.14 (12.38) Arm4: 0.177 (15.91); P=0.079	NR	NR (Authors report that there were no serious adverse events.)

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Recio-Mayoral, 2007 [49]	Arm1: Oral NAC post–contrast + IV normal saline Arm2: IV NAC pre-contrast oral NAC post-contrast+ IV sodium bicarbonate in 5% glucose and water	Primary endpoint: SrCr ≥ 0.5 mg/dl within 72 hours Arm1: 12/55 (21.8) Arm2: 1/56 (1.8); P=0.0009 OR 0.065 (95% CI, 0.008 to 0.521, P = 0.01) for Arm2. SrCr >25% within 72 hours Arm1: 17/55 (30.9) Arm2: 1/56 (1.8); P<0.0001 SrCr > 50% within 72 hours Arm1: 8/55 (14.5) Arm2: 0/56 (0); P=0.003	NR	At 7 days Arm1: 4/55 (7.3) Arm2: 1/56 (1.8); P=0.21	At 7 days Arm1: 3/55 (5.5) Arm2: 1/56 (1.8); P=0.36	NR	NR	Acute pulmonary edema/heart failure (during catheterization): Arm1: 2 (3.6) Arm2: 1 (1.8); P=0.62

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Reinecke, 2007 [50]	Arm1: IV normal saline +5% glucose Arm2: One session of hemodialysis + IV normal saline + 5% glucose Arm3: Oral NAC + IV normal saline + 5% glucose	SrCr ≥0.5 mg/dl At 24 hours Arm1: 8/137 (5.8) Arm2: 7/135 (5.2) Arm3: 4/140 (2.9); P=0.461 Within 72 hours Arm1: 7/115 (6.1) Arm2: 18/113 (15.9) Arm3: 6/114 (5.3); P=0.008 At 30-60 days Arm1: 6/125 (4.8) Arm2: 6/118 (5.1) Arm3: 4/129 (3.1); P=0.704	Incidence of CIN (SrCr ≥ 0.5 mg/dl) in the following subgroups: Diabetics: Time point NR Arm1: (13.3) Arm2: (18.4) Arm3: (9.7); P=0.577 Non-Diabetics: Time point NR Arm1: (3.5) Arm2: (14.7) Arm3: (3..6); P=0.007 SrCr <2mg/dl Time point NR Arm1: (5.7) Arm2: (14.0) Arm3: (2.9); P=0.009 SrCr ≥2mg/dl Time point: NR Arm1: (10.0) Arm2: (2.05) Arm3: (17.3); P=0.570 Stage 3 CKD (GFR 30-59 ml/min) Cr >0.5 mg/dl Time point: 72 hours Arm1: (5.9) Arm2: (16.0) Arm3: (4.1); P=0.007	In-hospital Arm1: 1/NR (0.7) Arm2: 3/NR (2.2) Arm3: 1/NR (0.7); P=0.427 30-Day Arm1: 3/NR (2.2) Arm2: 3/NR (2.2) Arm3: 1/NR (0.7); P=0.540 Long-Term mortality, deaths per 100 patient-years (median long-term follow-up: 553 days, with range 63 to 1316 days), Arm1: 9.7 Arm2: 13.1 Arm3: 9.9; P=0.582	In-hospital Time point: NR Arm1: 1/NR (0.7) Arm2: 2/NR (1.5) Arm3: 1/NR (0.7); P=0.762	Mean (95% CI) At 24 hours: Arm1: 0.10 (0.06, 0.13) Arm2: 0.12 (0.07, 0.17) Arm3: 0.11 (0.06, 0.15); P=0.838 At 72 hours: Arm1: 0.14 (0.09, 0.18) Arm2: 0.28 (0.18, 0.38) Arm3: 0.24 (0.16, 0.32); P=0.094 At 30-60 days: Arm1: -0.09 (-0.16, -0.01) Arm2: -0.07 (-0.15, 0.01) Arm3: -0.10 (-0.16, -0.03); P=0.639	NR	NR

Evidence Table E. Summary of all outcomes reported in studies comparing N-acetylcysteine versus other interventions for the prevention of contrast-induced nephropathy (continued)

*Divide SrCr presented as micromol/liter by 88.4 to obtain mg/ml; %=percent; AMI=acute myocardial infarction; CI=confidence interval; Cr=creatinine; CrCl=creatinine clearance; CIN=contrast induced nephropathy; dL=deciliter; IV=intravenous; LVEF=Left Ventricular Ejection Fraction; mg=milligram; ml/kg=milliliter per kilogram; ml/min=milliliter per minute; N=sample size; NAC=N-acetylcysteine;; NaHCO3=sodium bicarbonate;; NR=not reported; OR=odds ratio; P=p-value; RRT=renal replacement therapy; SD=standard deviation; SrCr: serum creatinine

*n/N refers to number of events divided by number at risk.

Evidence Table F. Summary of studies comparing sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N	Population included	Age, range of means§	No. female (%)‡	Mean followup	CM route*	Definition of CIN*	Study limitations†
Adolph, 2008[3]	NaCl + 5% dextrose vs. NaHCO3 + 5% dextrose	145	Two Cr concentration levels >106 m mol/l (>1.2mg/dl) within 12 weeks before coronary angiography	70-73	32 (22)	48 hours	IOCM (Iodixanol) IA	A3	M
Cho, 2010[14]	IV Normal Saline vs. IV Normal Saline + NaHCO3 vs. oral fluids vs. oral fluids + NaHCO3	91	General	77-81	45 (49)	72 hours	LOCM (Isoversol) IA	A3	M
Klima, 2012[29]	Normal Saline vs LT NaHCO3 vs. ST NaHCO3	258	>93 umol/L for women and >117 umol/L for men or estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m2	69-81	92(36)	48 hours	LOCM, IOCM IA or IV	A3	M
Pakfetrat, 2009[47]	Normal Saline + dextrose vs. NaHCO3 + dextrose vs. acetazolamide	286	General	58-59	111 (39)	48 hours	IOCM (Iodixanol) IA	RIFLE criteria	M
Tamura, 2009[72]	Normal Saline vs. Normal Saline+ NaHCO3	144	Cr level >1.1 to <2.0 mg/dl	72-73	18 (13)	7 days	LOCM (Iohexol) IA	A3	M

CIN=contrast induced nephropathy; Cr=creatinine; eGFR=estimated glomerular filtration rate; H=high risk; IA=Intrarterial; IOCM=iso-osmolar contrast media; IV=intravenous; L=low risk; LOCM=low osmolar contrast media; LT=long term; M=moderate risk; Mg/dl=milligram per deciliter; Mmol/l=millimole per liter; N=sample size; NaCl=sodium chloride; NaHCO3=sodium bicarbonate; ST=short-term; Umol/l=micromole per liter

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Percent females in entire study population
§ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table G. Summary of all outcomes reported in studies comparing sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Adolph, 2008[3]	Arm1: sodium chloride in 5% dextrose Arm2: sodium bicarbonate in 5% dextrose	Increase is Cr beyond 0.5mg/dl or 25% Time point: 48 hours Arm1: 2/74 (2.7) Arm2: 3/71 (4.2) All arms p=0.614	NR	NR	NR	Cr, short-term (mg/dL) Time point: 48 hours Arm1: 1.59 (0.40) Arm2: 1.56 (0.52) All arms p=0.33	NR	NR	NR

Evidence Table G. Summary of all outcomes reported in studies comparing sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Cho, 2010[14]	Arm1: IV Normal Saline Arm2: IV NS + bicarb Arm3: oral fluids Arm4: oral fluids + NaHC3	Cr increase >25% or rise 0.5 mg/dL Time point: 72 hours Arm1: 6/27 (22) Arm2: 2/21 (18.2) Arm3: 1/22 (4.5) Arm4: 1/21 (4.8) Arm1 vs. Arm2 P=0.784 Arm1 vs. Arm3 P=0.617 Arm1 vs. Arm4 P=0.342 Arm2 vs. Arm3 P=0.835 Arm2 vs. Arm4 P=0.525	NR	NR	NR	NR	NR	Arm1: 4.18 Arm2: 4.09 Arm3: 4.36 Arm4: 6.9	NR

Evidence Table G. Summary of all outcomes reported in studies comparing sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Klima, 2012[29]	Arm1: Normal Saline Arm2: long-term sodium bicarbonate Arm3: short-term sodium bicarbonate	NR	Cr increase ≥44 umol/l Time point: 48 hours Arm1: 1/89 (1) Arm2: 7/87 (8) Arm3: 6/82 (7) All arms, p=0.03 Cr increase ≥25% Time point: 48 hours Arm1: 1/89 (1) Arm2: 8/87 (9) Arm3: 8/82 (10) All arms p=0.02	NR	NR	Change in Cr from baseline, umol/l Time point: 48 hours Arm1: -7 Arm2: + 3 Arm3: -2	NR	NR	NR

Evidence Table G. Summary of all outcomes reported in studies comparing sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Pakfetrat, 2009[47]	Arm1: Normal Saline Arm2: sodium bicarbonate in dextrose solution Arm3: sodium chloride + acetazolamide	Rifle criteria Time point: 48 hours Arm1: 16/96 (16.6) Arm2: 4/96 (4.2) Arm3: 5/94 (5.3 All arms P=0.04	NR	NR	NR	Cr, short-term (mg/dL) Time point: 48 hours Arm1: 1.1 (0.2) Arm2: 1.1 (0.3) Arm3: 1.1 (0.3)	NR	NR	NR
Tamura, 2009[72]	Arm1: IV Normal Saline Arm2: IV Normal Saline+ sodium bicarbonate	Increase >25% or >0.5 mg/dl in Cr Time point: 3 days Arm1: 9/72 (12.5) Arm2: 1/72 (1.4) All arms P=0.017	NR	NR	NR	Cr, short-term (mg/dL) Time point: 3 days Arm1: 1.38 (0.19) Arm2: 1.36 (0.18) All arms P=0.49	NR	NR	NR

%=percent; CIN=contrast induced nephropathy; IV=intravenous; IVF=intravenous fluid; Mg/dl=milligram per deciliter; N=sample size; NaHCO3=sodium bicarbonate; NR=not reported;; P=P-value; RRT=renal replacement therapy; SD=standard deviation; Umol/l=micomole per liter; Cr=creatinine

*n/N refers to number of events divided by number at risk.

Evidence Table H. Summary of studies comparing N-acetylcysteine plus sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N	Population included	Age, range of means‖	No. female (%)¶	Mean followup	CM Route	Definition of CIN*	Study limitations†
Briguori, 2007[11]	NormS + NAC vs. NaHCO3 + NAC vs. NormS + ascorbic acid + NAC	326	CKD with stable Cr at 2.0 mg/dL and/or estimated glomerular filtration rate 40	71-70	57 (17)	7 days	IOCM (Iodixanol) IA	A1	M
Briguori, 2011[12]	NaHCO3 in dextrose + NAC vs. RenalGuard: (NS+ NAC + furosemide)	292	CKD (eGFR <30)	76	101 (34)	1 month	IOCM (Iodixanol) IA	Increase in Cr >0.3mg‡	L
Heguilen, 2013[24]	NaHCO3 + dextrose v NaHCO3 + NAC +dextrose v NaCl + NAC+dextrose	133	Stable Cr ≥ 1.25 mg/dl, or Cockcroft-Gault-estimated CrCl (eCrC) <45 ml/min	64-67	31 (25)	48-72 hours (labs checked in that time frame; not all at 3 days)	LOCM (Ioversol) IA	A1	M
Heng, 2008[73]	NaHCO3 vs. NaHCO3 + NAC	60	Chronic renal failure, GFR < 56 ml/min, stable Cr concentrations	71-72	13 (21)	48 hours	IOCM (Iodixanol), LOCM (Iomeprol) IA	A1	H
Maioli, 2008[38]	NormS + NAC vs. NaHCO3 + NAC	502	Chronic kidney dysfunction, creatinine clearance < 60 ml./min	74	206 (41)	10 days (Cr also checked a1 month in cases of CIN from earlier time points)	IOCM (Iodixanol) IA	A1 §	L
Ratcliffe, 2009[48]	NaCl +dextrose vs. NaCl + NAC +dextrose vs. NaHCO3+dextrose vs. NaHCO3 a + NAC+dextrose	78	Renal insufficients, Cr Men >132.6 mg/dL Women >114.9 mg/dL and/or diabetics	64-68	31 (39)	7 days	IOCM (Iodixanol) IA	A1	H
Staniloae, 2009[74]	NaHCO3 v NAC+NaHCO3	414	Moderate-to-severe chronic kidney disease with eGFR of 20-59ml/min per 1.73 m^2	149 (36)	71	7 Days	Iodixanol, Iopamidol IA	A2	M

CIN=contrast induced nephropathy; CM=contrast media; Cr=creatinine; CrCl=creatinine clearance; eCrC=estimated creatinine clearance; eGFR=estimated glomerular filtration rate; H=high risk; IA=intrarterial; IV=intravenous; L=low risk; M=moderate risk; mg/dl=milligram per deciliter; N=sample size; NAC=N-acetylcysteine; NaCl=sodium chloride; NaHCO3=sodium bicarbonate; NormS=normal saline; vs.=versus

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4). B: >25% reduction in creatinine clearance.
† Study limitations: L=low risk of bias; M=moderate risk of bias; H =high risk of bias
‡ increase of serum creatinine >25% was secondary outcome
§CIN outcomes also assessed at 48 hours.
¶ Percent females in entire study population
‖ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table I. Summary of all outcomes reported in studies comparing N-acetylcysteine plus sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy

Author, year	Comparison	Incidence of CIN, n/N (%)*	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)	Need for RRT, n/N (%)	Change in serum creatinine, mean (SD)	Prolonged hospitalization, mean days (SD)	Cardiac events, n/N (%)
Briguori, 2007[11]	Arm2: NormS+ NAC Arm3: NaHCO3 + NAC Arm4: NormS + ascorbic acid + NAC	Cr >25% at 48 hours Arm2: 11 (9.9) Arm3: 2 (1.9) Arm4: 10 (10.3) Arm2 vs. Arm3 P=0.019 Arm2 vs. Arm4 P>0.05 P>0.05	NR	NR	NR	NR	NR	NR

Evidence Table I. Summary of all outcomes reported in studies comparing N-acetylcysteine plus sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)*	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)	Need for RRT, n/N (%)	Change in serum creatinine, mean (SD)	Prolonged hospitalization, mean days (SD)	Cardiac events, n/N (%)
Briguori, 2007[11] (continued)		eGFR increase >25% Arm2: 10 (9.2) Arm3: 1 (0.9) Arm4: 12 (11.2) Arm2 vs. Arm3 P<0.009 Arm2 vs. Arm4 P>0.05 Cr change >0.5mg Arm2: 12 (10.8) Arm3: 1 (0.9) Arm4: 12 (11.2) Arm2 vs. Arm3 P<0.003 Arm2 vs. Arm4 P>0.05 Arm4						

Evidence Table I. Summary of all outcomes reported in studies comparing N-acetylcysteine plus sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)*	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)	Need for RRT, n/N (%)	Change in serum creatinine, mean (SD)	Prolonged hospitalization, mean days (SD)	Cardiac events, n/N (%)
Briguori, 2011[12]	Arm1: NAC + NaHCO3 Arm2: NormS+NAC+RenalGuard group	At 48 hours Cr >0.3mg 48 hours Arm1: 30 (20.5%) Arm2: 16 (11%) P=0.025 Cr >25% Arm1: 19(13) Arm2: 4(2.7) P=NR Cr >50% Arm1: 11 (7.5) Arm2: 1 (0.7) P=NR Cr >0.5mg Arm1: 22 (15) Arm2: 9 (6) P=NR	CR> 0.3mg at 48 hours GFR <30 Arm1: 20 (29.5%) Arm2: 11 (15%) P=NR CI-AKI Risk score >11 Arm1: 11 (14%) Arm2: 5 (7%)	Long-term Arm1: 6 (4.1) Arm2: 6 (4.1) P=1.0	Long-term Arm1: 7 (4.8) Arm2: 1 (0.7) P=0.03	At 48 hours Arm1: 0.14 (0.46) Arm2: -0.05 (0.32) P<0.001	NR	Acute pulmonary edema Arm1: 1(0.7) Arm2: 3(2.1) P=0.62
Heguilen, 2013[24]	Arm1: NaHCO3 + dextrose Arm2: NaHCO3 + NAC +dextrose Arm3: NaCl + NAC+dextrose	Cr >25% Arm1: 15(35.7) Arm 2: 3(7.0) Arm3: 6(15.8) P<0.001	NR	Arm1 vs. Arm2 vs. Arm3 P=NS	Arm1 vs. Arm2 vs. Arm3 P=NS	NR	Arm1 vs. Arm2 vs. Arm3 P=NS	NR

Evidence Table I. Summary of all outcomes reported in studies comparing N-acetylcysteine plus sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)*	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)	Need for RRT, n/N (%)	Change in serum creatinine, mean (SD)	Prolonged hospitalization, mean days (SD)	Cardiac events, n/N (%)
Heng, 2008[73]	Arm1: Placebo Arm2: NAC + NaHCO3	At 48 hours Cr >44µmol/L Arm1: 2 (6.3) Arm2: 0 (0) P=0.49 Cr >25% Arm1: 2(6.3) Arm2: 1(3.5) P=1 Decrease in GFR by 5ml/min Arm1: 3(9.3) Arm2: 2(7.1) P=1	NR	NR	Arm1: 0 (0) Arm2: 0 (0)	At 48 hours Arm1: -3 (28) Arm2: -2 (25) P=0.84	NR	Time NR Congestive heart failure Arm1: 0(0) Arm2: 1(3.6) P=NR
Maioli, 2008[38]	Arm2: NormS+ NAC Arm3: NAC + NaHCO3	Cr >25% 5 days Arm2: 29(11.5) Arm3: 25(10) P=0.60 48 hours Arm2: 25(10.0) Arm3: 38(15.1) P=0.09	NR	NR	NR	NR	NR	NR

Evidence Table I. Summary of all outcomes reported in studies comparing N-acetylcysteine plus sodium bicarbonate versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)*	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)	Need for RRT, n/N (%)	Change in serum creatinine, mean (SD)	Prolonged hospitalization, mean days (SD)	Cardiac events, n/N (%)
Ratcliffe, 2009 [48]	Arm1: NaCl +dextrose Arm2: NaCl + NAC +dextrose Arm3: NaHCO3 +dextrose Arm4: NaHCO + NAC+dextrose	Cr >25% at 72 hours Arm1: 1 (7) Arm2: 1 (5) Arm3: 2 (11) Arm4: 1 (4) P=0.86	NR	NR	NR	72 hours µmol/L Arm1: 6.19 (30.1) Arm2: 7.1 (13.2) Arm3: 8.0 (15.0) Arm4: -1.8 (14.1) P=0.29 Maximum change µmol/L Arm1: 10.6 (29.2) Arm2: 9.7 (13.2) Arm3: 14.1 (12.4) Arm4: 0.2 (15.9) P=0.08	NR	NR
Staniloae, 2009 [74]	Arm1: NaHCO3 Arm2: NaHCO3 + NAC	Cr >25% Arm1: 26(10.6) Arm2: 20(11.9 P=0.75 eGFR >25% Arm1: 21(8.5) Arm2: 12(7.1) P=0.71 Cr change >0.5mg Arm1: 16(6.5) Arm2: 7(4.2) P=0.38	NR	NR	NR	48-72 hours Arm1: 0.11 (0.23) Arm2: 0.07 (0.21) P=0.14	NR	NR

%=percent; CIN=contrast induced nephropathy; CKD=chronic kidney disease; CM=contrast media; F=female; IA=Intrartieral; IOCM=iso-osmolar contrast media; IV=intravenous; LOCM=low osmolar contrast media; mg/dl=milligram per deciliter; N=sample size; NAC=N-acetylcysteine; NormS=normal saline; vs.=versus; Cr=creatinine

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Percent females in entire study population
§ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table J. Adverse events in studies comparing of N-acetylcysteine plus sodium bicarbonate versus other interventions

Author, Year	Adverse events
Briguori, 2007[11]	NR
Briguori, 2011[12]	Other: Mortality; Deaths at 1 month post procedure; Acute pulmonary edema; at 1 month post procedure
Heguilen, 2013[24]	NR
Heng, 2008[73]	Two participants (one from each arm) developed diarrhea.
Maioli, 2008[38]	Heart failure: 5 patients had acute cardiac failure resulting in death; Anaphalaxis; Infective multi organ failure: 1 patient had this event resulting in death
Ratcliffe, 2009[48]	No serious adverse events from any of the medications given or from the procedure itself
Staniloae, 2009[74]	NR

NR=not reported

Evidence Table K. Summary of studies comparing diuretics versus other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N	Population	Age, Range of means§	Mean followup	Procedure	CM	Definition of CIN*	Study limitations†
Marenzi, 2012[41]	Normal saline vs. Normal saline + furosemide (furosemide bolus up to 50mg)	170	Inclusion eGFR <60 ml/min/1.73 m^2 CKD stages 3-4 NYHA < IV	61-90	72 hours	Urgent or elective coronary angiography w/ or w/o PCI	LOCM Iomeprol	A3	M
Pakfetrat, 2009[47]	Normal saline vs. bicarbonate vs. Normal saline + acetazolamide	286	All patients undergoing coronary intervention	46–68	48 hours	Coronary angiography w/ or w/o PCI	IOCM Iodixanol	Rifle criteria	M
Solomon, 1994[53]	0.45% saline vs. 0.45% saline + furosemide vs. 0.45% saline + mannitol (furosemide infusion up to 80mg)	78	Cr >1.6 mg/dl/ eGFR <60 ml/min/1.73 m^2	50-78	48 hours	Coronary angiography	LOCM Iopentol	A2	L

CKD=Chronic Kidney Disease; CIM=Contrast induced nephropathy; CM=Contrast media; Cr=creatinine; CrCl=Creatinine Clearance; eGFR=estimated glomular filtration rate; HOCM=high-osmolar contrast media; IOCM=iso-osmolar contrast media; LOCM=low-osmolar contrast media; NYHA=New York health association; PCI=Percutaneous coronary intervention; RCT=Randomized Controlled Trial

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡RIFLE criteria: (at 48 hours), Scr increase x 1.5 or GFR decrease > 25% from baseline + urine output <5ml/kg/h x 6h
§ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table L. Summary of all outcomes reported in studies of diuretics versus other interventions for the prevention of contrast-induced nephropathy

Author, year	Comparison	Incidence of CIN n/N (%)*	Clinical events n/N (%)	Mortality n/N (%)	Need for RRT n/N (%)	Cardiac events, n/N (%)
Marenzi, 2012[41]	Arm 1: Normal saline Arm 2:Normal saline + furosemide	Overall Arm1: 15/83 (18%) Arm2: 4/87 (4.6%) P=0.005, RR=0.29 CIN in patients with elective procedures Arm1: 5/52 (10%) Arm2: 2/48 (4%) P=0.44, RR=0.42 CIN in patients with urgent procedures Arm1: 10/31 (32%) Arm2: 2/39 (5%) P=0.003, RR=0.16	In-hospital complications Arm1: 7 (8%) Arm2: 15 (18%) P=0.052 Acute pulmonary edema Arm1: 5 (6%) Arm2: 10 (12%) P=0.15 Acute myocardial infarction Arm1: 0 (-) Arm2: 1 (1.2%) P =0.30 Atrial fibrillation Arm1: 1 (1.1%) Arm2: 2 (2.4%) P=0.53	In-hospital death Arm1: 1 (1.1%) Arm2: 3 (4%) P=0.29	Arm1: 3 (4%) Arm2: 1 (1%) P=0.29	AMI Arm1: 1/83 (1.2) Arm2: 0/87 (0) P=0.30
Pakfetrat, 2009[47]	Arm 1: Normal saline Arm 2: bicarbonate Arm 3: Normal saline + acetazolamide	Risk Arm1: 12 (12.5%) Arm2: 4 (4.2%) Arm3: 5 (5.3%) P=0.04 Injury Arm1: 3 (1%) Arm2: 0 (-) Arm3: 0 (-) P=0.05 Failure Arm1: 1 (0.3%) Arm2: 0 (-) Arm3: 0 (-) P=0.37	No events	No events	No events	

Evidence Table L. Summary of all outcomes reported in studies of diuretics versus other interventions for the prevention of contrast-induced nephropathy (continued)

Author, year	Comparison	Incidence of CIN n/N (%)*	Clinical events n/N (%)	Mortality n/N (%)	Need for RRT n/N (%)
Solomon, 1994[53]	Arm 1: 0.45% saline Arm 2: 0.45% saline + furosemide Arm 3: 0.45% saline. + mannitol	Arm1: 3/28 (11%) Arm2: 10/25 (40%) 7/25 (28%) P=0.05 CIN in diabetic (n=13) Arm1: 2 /14 (14%) Arm2: 6/14 (43%) Arm3: 5/13 (38%) P =NS CIN in non-diabetic (n=7) Arm1: 1/14 (7%) Arm2: 4/11 (36%) Arm3: 2/12 (17%) P=NS	Length of hospitalization + 4 days in CIN patients	NR	Arm1: 0/28 Arm2: 1/25 Arm3: 0/25

AMI=acute myocardial infarction; CHF=chronic heart failure; CIN=contrast induced nephropathy; NR=not reported; RR=relative risk; RRT=renal replacement therapy

*n/N; number of events/population at risk (patients in arm)

Evidence Table M. Summary of the characteristics of studies comparing vasoactive agents with other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparators	N	Population	Age, range of means‡	Procedure / CM	Definition of CIN*	Hydration and duration	Vasodilator dose and duration	Study limitations†
Allaqaband, 2002[5]	0.45% saline vs. 0.45% saline + fenoldopam vs. 0.45% saline + NAC	123	Cr ≥ 1.6 mg/dl	70-71	Cardiovascular interventions LOCM	A2	Saline 0.45%, 24 hours (12 hours before-12 hours after)	NAC 600 mg PO X2 12 h before-12 hours after (total 1200mg) Fenoldopam 0.1mcg/kg/min infusion for 8 hours (4 hours before, 4 hours after CM)	M
Briguori, 2004[9]	0.45% saline + fenoldopam vs. 0.45% saline + NAC	192	Cr >1.5 mg/dl or CrCl <60ml/min	68-69	Coronary and/or peripheral angiography IOCM	A2	Saline 0.45% 24 hours (12 hours before-12 hours after)	NAC 1200 mg PO bid x 2 days (the day before and the day of the procedure) (total 4800mg) Fenoldopam 0.1mcg/kg/min infusion starting 1 hour before CM and for 12 hours after.	M
Demir, 2008[15]	Normal saline vs. Normal saline + nifedipine vs Normal saline + NAC vs Normal saline + misoprostol vs. Normal saline + theophylline	97	Stable renal disease Cr >1.2mg/dl	43-77	Computed tomography LOCM	A3	Saline 0.9% 2000ml	Nifedipine 30 mg/day for 5 days starting 3 days before the procedure	H
Gunebakmaz, 2012[20]	Normal saline vs. Normal saline+ nevibolol vs. Normal saline + NAC	120	Cr ≥ 1.2mg/dl	53-66	Cardiovascular interventions IOCM	A3	Saline 0.9% 1ml/kg/h infusion for 82h (6 hours before, 12 hours after)	Nevibolol 5mg day for 4 days starting 2 days before procedure	H
Li, 2011[36]	Normal saline vs. Normal saline+ benazepril	114	Mild or moderate CKD CrCl ≥60ml/min ≤89 ml/min	52-72	Coronary interventions LOCM	A3	Saline 0.9% 1ml/kg/h infusion for 12h (6 hours before, 6 hours after)	Benazepril 10mg/day, 3 days, Prior to CM administration	H

Evidence Table M. Summary of the characteristics of studies comparing vasoactive agents with other interventions for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparators	N	Population	Age, range of means‡	Procedure / CM	Definition of CIN*	Hydration and duration	Vasodilator dose and duration	Study limitations†
Ng, 2006[44]	Normal saline + fenoldopam vs. Normal saline + NAC	95	Cr >1.5 mg/dl or CrCl <60ml/min	57-80	Coronary angiography IOCM, LOCM	A3	Saline 0.9% 1ml/kg/ starting 1-2 hours before continuing 6-12 hours after	NAC 600 mg PO bid x 2 days (the day before and the day of the procedure) (total 2400mg) Fenoldopam 0.1mcg/kg/min infusion for 8 hours (2 hours before, 6 hours after CM)	M
Oguzhan, 2013[45]	Normal saline vs. Normal saline + amlodipin-valsartan	90	Cr <2.1 mg/dl	62-66	Coronary arteriography and ventriculography LOCM	A3	Saline 0.9% 24 hours (12 hours before, 12 hours after)	Amlodipine-valsartan 5/160mg x3 (24h before the procedure-the day of the procedure and 24 hours after)	H
Talati, 2012[55]	Intra renal fenoldopam +hydration (not specified) vs. matched control (NAC) + hydration (not specified)	52	Coronary procedurees	69	Cardiovascular interventions IOCM	A3	No mention of hydration protocol	NAC 1200 mg 4 doses PO (2 before, 2 after) (total 4800mg) Fenoldopam 0.1-0.4mcg/kg/min intrarenal	H

CIN=contrast induced nephropathy; CM=contrast media; IOCM-ios-osmolar contrast media; Cr=creatinine; LOCM=low-osmolar contrast media; NAC=n-acetylcysteine; PO=per os

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4). B: >25% reduction in creatinine clearance.
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table N. Summary of the outcomes of studies comparing vasoactive agents versus other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	Incidence of CIN n/N (%)*	Clinical events n/N (%)	Mortality n/N (%)	Need for RRT n/N (%)
Allaqaband, 2002[5]	Arm 1: 0.45% saline Arm 2: 0.45% saline + fenoldopam Arm 3: 0.45% saline + NAC	Overall (N=20) Arm1: 15.3% Arm2: 15.7% Arm3: 17.7% P=0.919 CIN in diabetes (Y/N) Arm1: 3/3 Arm2: 5/3 Arm3: 4/2 P=0.813	NR	NR	2 of the 20 patients developing CIN required HD (not reported by group)
Briguori, 2004[9]	Arm 1: 0.45% saline + fenoldopam Arm 2: 0.45% saline + NAC	Overall Arm1: 13/95 (13.7%) Arm2: 4/97 (4.1%) P=0.019, OR=0.27 (0.08-0.85) CIN in diabetic patients Arm1: 5/11 (45%) Arm2: 1/9 (11%) P=0.095 CIN in patients with Cr >2.5 Arm1: 27/135 (20%) Arm2: 11/140 (7.9%) P=0.005	Length of hospitalization Arm1: 5.0 +/- 10 Arm2: 2.9 +/- 2.7 P=0.049	Arm1: 1 (1.1%) Arm2: 0 (-)	Arm1: 1 (1.1%) Arm2: 0 (-)
Demir, 2008[15]	Arm 1: Normal saline vs. Arm 2: Normal saline + nifedipine Arm 3: Normal saline + NAC Arm 4: Normal saline + misoprostol Arm 5: Normal saline + theophylline	Arm1: 0/20 (-) Arm2: 0/17 (-) Arm3: 1/20 (5%) Arm4: 0/20 (-) Arm5: 4/20 (20%	No difference in length of hospitalization	NR	Arm1: 0 Arm2: 0 Arm3: 0 Arm4: 0 Arm5: 0
Gunebakmaz, 2012[20]	Arm 1: Normal saline vs. Arm 2: Normal saline+ nevibolol Arm 3: Normal saline + NAC	Arm1: 11 (27.5%) Arm2: 8 (20%) Arm3: 9 (22.5% P=0.72	NR	NR	NR
Li, 2011[36]	Arm 1: Normal saline Arm 2: Normal saline+ benazepril	Arm1: 9.7% Arm2: 3.5% P=0.506	NR	NR	NR

Evidence Table N. Summary of the outcomes of studies comparing vasoactive agents versus other interventions for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	Incidence of CIN n/N (%)*	Clinical events n/N (%)	Mortality n/N (%)	Need for RRT n/N (%)
Ng, 2006[44]	Arm 1: Normal saline + fenoldopam Arm 2: Normal saline + NAC	Overall Arm1: 8/40 (20%) Arm2: 5/44 (11.4%) P=0.4 No association after adjusting for diabetes, CHF and gender P=0.3	Length of hospitalization + 4 days in CIN patients	NR	NR
Oguzhan, 2013[45]	Arm 1: Normal saline Arm 2: Normal saline + amlodipin-valsartan	Arm1: 3 (6.7%) Arm2: 8 (17.8%) P=0.197	NR	NR	0 0
Talati, 2012[55]	Arm 1: Intra renal fenoldopam +hydration (not specified) Arm 2: matched control (NAC) + hydration (not specified)	Arm1: 6/52 (11.5%) Arm: 16/52 (30%) P=0.012 RR 0.38 95%CI 0.16-0.88)	Length of hospitalization in CIN patients Arm1: 5.7 + /- 4.6 Arm2: 8.1 + /- 6.1 P=0.39	Arm1: 0 Arm2: 1 P=0.52	Arm1: 0 Arm2: 3 P=0.52

CHF=congestive heart failure; CI=confidence interval; CIN=contrast induced nephropathy; Cr=creatinine; HD=hemodialysis; NAC=n-acetylcysteine; RRT=renal replacement therapy

*n/N; number of events/population at risk (patients in arm)

Evidence Table O. Adverse events in studies comparing vasoactive agents versus other interventions for the prevention of contrast induced nephropathy

Author, Year	Adverse events
Allaqaband,2002[5]	Other: Hypotension; Fenoldopam reaction. Definition not reported
Briguori,2004[9]	Other: Hypotension; Allergic reaction; skin rash and vomiting
Demir,2008[15]	NR
Gunebakmaz, 2012[20]	NR
Li, 2011[36]	NR
Ng, 2006[44]	No patient had any adverse event in any arm
Oguzhan, 2013[45]	NR
Talati, 2012[55]	Other: Hypotension; NR

NR=not reported

Evidence Table P. Summary of the characteristics and outcomes of studies comparing antioxidants versus hydration for the prevention of contrast-induced nephropathy

Author, year	Comparisons	N	Procedure / CM	Definition of CIN*	Hydration and duration	Agent dose and duration	Study limitations†
Firouzi, 2012[17]	Normal saline vs. Normal saline + pentoxifylline	286	Coronary angioplasty LOCM	A3	Saline 0.45% 1ml/kg/ 12 hours (6 hours before, 6 hours after)	400mg PO 3 x day for 48 hours starting 24 hours before CM	H
Kimmel, 2008[27]	0.45% saline+ placebo vs. 0.45% saline +NAC vs. 0.45% saline + zinc	54	Coronary angiography w/ or w/o PCI LOCM	A3	Saline 0.45% 1ml/kg/ 24 hours (12 hours before, 12 hours after)	NAC 600 mg PO bid x 2 days (total 2400mg) Zinc 60mg PO 24 hours before CM	M
Li, 2009[35]	Normal saline vs. Normal saline + probucol	205	Coronary angiography w/ or w/o PCI LOCM	A3	Saline 0.9% 1ml/kg/ 12 hours after	Probucol 500mg PO before procedure-then 500mg PO bid for 3 days	H
Ludwig, 2011[37]	Normal saline + placebo vs. Normal saline + MESNA	100	Coronary and peripheral angiography-CT LOCM	A1	Saline 0.9% 1000 ml before and 500 ml after CM	MESNA 1600mg IV (in 500 ml saline) immediately before procedure	L
Yin, 2013[59]	Arm1: No probucol Arm2: Probucol	204	Primary or urgent coronary angioplasty	A3	Saline 0.9% 1mlm/kg/ 24 hours	Probucol 1000mg before procedure and 500mg twice daily after	M

Bid=*bis in die*; CIN=contrast induced nephropathy; CM=contrast media; CT=computerized tomography; def=definition; IV=intravenous; LOCM=low-osmolar contrast media; MESNA= sodium 2-mercaptoethanesulfonate; ml/kg/hours=milliliter per kilogram per hour; Ml=milliliter; N=sample size; NAC=N-acetylcysteine; NS=non-significant; p=p-value; PCI=percutaneous coronary intervention; PO=*per os*; Vs=versus; w/=with; w/o=without

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡n/N; number of events/population at risk (patients in arm)

Evidence Table Q. Summary of the characteristics and outcomes of studies comparing either misoprostol or angiotensin blockers versus hydration for the prevention of contrast-induced nephropathy

Author, year	Comparisons	N	Procedure / CM	Definition of CIN*	Hydration and duration	Agent dose and duration	Study limitations†
Demir, 2008[15]	Normal saline vs. Normal saline + misoprostol vs. Normal saline + NAC vs. Normal saline + theophylline vs. Normal saline + nifedipine	97	Computed tomography LOCM	A3	Saline 0.9% 2000ml	Misoprostol 200mg, bid, 3 days prior, day of, 1 day post procedure	H
Rosenstock, 2008[51]	Naïve to angiotensin blockade vs. Continue angiotensin blockade during and after procedure vs Discontinue angiotensine blockade morning of procedure and 24hrs after procedure	283	Coronary angiography	A3	Dose and duration not reported	Dose and duration not reported	H

bid=*bis in die*; CIN=contrast induced nephropathy; CM=contrast media; Hrs=hours; LOCM=low-osmolar contrast media; mg=milligram; ml=millimeter; N=total sample size; NAC=N-acetylcysteine; vs=versus

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡n/N; number of events/population at risk (patients in arm)

Evidence Table R. Summary of all outcomes reported in studies comparing antioxidants versus hydration for the prevention of contrast-induced nephropathy

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Firouzi, 2012[17]	Arm1: Normal saline Arm2: Normal saline + pentoxifylline	Arm1: 20/146 (13.7) Arm2: 12/140 (8.5) P=0.17	NR	48 hours Arm1: 0/146 (0) Arm2: 0/140 (0) P=NR	48 hours Arm1: 0/146 (0) Arm2: 0/140 (0) P=NR	NR	NR
Kimmel, 2008[27]	Arm1: 0.45% saline+ placebo Arm2: 0.45% saline +NAC Arm3: 0.45% saline + zinc	Arm1: 1/17 (6) Arm2: 1/19 (5) Arm3: 2/18 (11) P=NS	CIN def: A1 Arm1: 2/17 (12) Arm2: 1/19 (5) Arm3: 3/18 (17) P=NS	NR	NR	NR	NR
Li, 2009[35]	Arm1: Normal saline Arm2: Normal saline + probucol	Arm1: 15/103 (14.56) Arm2: 8/102 (7.84) P=0.13	NR	NR	NR	NR	NR
Ludwig, 2011[37]	Arm1: Normal saline + placebo Arm2: Normal saline + MESNA	Arm1: 7/49 (14) Arm2: 0 (0) P=0.005	NR	NR	NR	NR	NR
Yin, 2013[59]	Arm1: No probucol Arm2: Probucol	At 72 hours Arm1: 23/108 (21.3) Arm2: 4/96 (4.2) P<0.001	NR	NR	NR	NR	NR

CIN=contrast induced nephropathy; Hrs=hours; MESNA= sodium 2-mercaptoethanesulfonate; n=number of patients with event; N=total sample size; NAC=N-acetylcysteine; NR=not reported; NS=not significant; P=p-value; RRT=renal replacement therapy; SD=standard deviation

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡n/N; number of events/population at risk (patients in arm)

Evidence Table S. Summary of all outcomes reported in studies comparing either misoprostol or angiotensin blockers versus hydration for the prevention of contrast-induced nephropathy

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)	Mortality, n/N (%)*	Need for RRT, n/N (%)	Length of hospital stay, mean days (SD)	Cardiac events, n/N (%)
Demir, 2008[15]	Arm1: Normal saline Arm2: Normal saline + misoprostol Arm3: Normal saline + NAC Arm4: Normal saline + theophylline Arm5: Normal saline + nifedipine	Arm1: 0/20 (0) Arm2: 0/20 (0) Arm3: 1/20 (5) Arm4: 4/20 (20) Arm5: 0/17 (0)	NR	NR	NR	NR	NR
Rosenstock, 2008[51]	Arm1: Naïve to angiotensin blockade Arm2: Continue angiotensin blockade during and after procedure Arm3: Discontinue angiotensine blockade morning of procedure and 24hrs after procedure	At 72 hours Arm1: 4/63 (6.3) Arm2: 7/113 (6.2) Arm3: 4/107 (3.7) P=0.66	NR	NR	72 hours Arm1: 0/63 (0) Arm2: 0/113 (0) Arm3: 1/107 (0) P=NR	NR	NR

CIN=contrast induced nephropathy; Hrs=hours; MESNA= sodium 2-mercaptoethanesulfonate; n=number of patients with event; N=total sample size; NAC=N-acetylcysteine; NR=not reported; NS=not significant; P=p-value; RRT=renal replacement therapy; SD=standard deviation

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡n/N; number of events/population at risk (patients in arm)

Evidence Table T. Summary of characteristics of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N	Population included	Age, range of means‡	Sex, n female (%)	Mean followup	CM Route*	Definition of CIN*	Study limitations†
Bader, 2004[7]	IV Saline infusion before and after procedure vs. IV saline infusion during procedure	39	General	64-65	7 (18)	48 hours	LOCM (Iohexol, Iopromide) IA	Decrease in GFR of >50% from the baseline GFR within 48 hours	H
Chen, 2008[13]	0.45% saline (normal kidney) vs. no hydration (normal kidney) vs. NAC + 0.45% saline (abnormal kidney) vs. NAC + no hydration (abnormal kidney)	936	Myocardial ischemia	60-63	149 (16)	6 months	IOCM IA	A2	H
Cho, 2010[14]	IV Normal saline vs. IV NaHCO3 + IV Normal saline vs. Oral Normal saline vs Oral Normal saline + Oral NAHCO3	91	General	78	45 (51)	NR	LOCM (Isoversol) IA	A3	M
Koc, 2012[30]	NAC + high-volume IV Normal saline vs. high-volume NAC + high-volume IV Normal saline vs. standard-volume IV Normal saline	220	CR ≥1.1 mg/dL or CrCl ≤60 mL/mi	62-65	50 (22)	48 hours	LOCM (Iohexol) IA	A3	H
Kong, 2012[31]	IV Normal saline vs. oral hydration before and after procedure vs oral hydration after procedure	120	General	54-57	53 (44)	6 months	LOCM (Iopromide) IA	A3	H
Krasuski, 2003[33]	0.45% saline + dextrose Normal salinevs. Normal saline	63	Moderate renal insufficiency	68-69	63 (17)	48 hours	NR IA	A2	H

Evidence Table T. Summary of characteristics of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	N	Population included	Age, range of means‡	Sex, n female (%)	Mean followup	CM Route*	Definition of CIN*	Study limitations†
Lawlor, 2007[34]	Oral Normal saline vs NAC + IV Normal saline vs. NAC + oral hydration Normal salineNormal saline	78	CrCl <50 mL/min	NR	24 (30)	48 hours	IA	A3	H
Maioli, 2011[39]	No hydration vs. late Normal saline vs early Normal salinesodium bicarbonate Normal saline	450	STEMI	64-66	120 (26)	48 hours	IOCM (Iodixanol) IA	A3	M
Marron, 2007[42]	Normal saline vs. 0.45% saline	71	General	64-68	23 (32)	30 days	IOCM (Iodixanol) IA	A1	H
Mueller, 2002[43]	Normal saline vs. 0.45% NaCl + 5% glucose	1383	General	64	354 (26)	30 days	LOCM IA	A2	H
Trivedi, 2003[56]	IV Normal saline vs. oral hydration	53	General	67-68	1 (1.8)	48 hours	LOCM IA	A2	H

GFR=glomular filtration rate; IA=intra-arterial; IOCM=iso-osmolar contrast media; ISO=isotonic; Cr=creatinine; CrCl=creatinine clearance IV=intravenous; LOCM-low-osmolar contrast media; NAC=N-acetyl cysteine.; NaCl=sodium chloride; NaHCO3=sodium bicarbonate; STEMI=ST segment elevation MI

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4). B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table U. Summary of the outcomes of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)*	Mortality n/N (%)	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days	Cardiac events, n/N (%)
Bader, 2004[7]	Arm1: IV saline infusion before and after procedure Arm2: IV saline infusion during procedure	eGFR ≥50% Time point: 48 hours Arm1: 1/19 (5.3) Arm2: 3/20 (15) All arms P=0.605	Diabetes Time point: 48 hours Arm1: 0/6 (0) Arm2: 1/4 (25) No Diabetes Time point: 48 hours Arm1: 1/13 (7.7) Arm2: 2/16 (12.5) RR: 0.35 (95% CI: 0.04-3.09, p=0.605; OR=0.31)	NR	Time point: NR Arm1: 0 Arm2: 0 P=NR	NR	NR	NR	NR
Chen, 2008[13]	Arm1: Normal renal function-non hydration Arm2: Normal renal function-0.45% saline Arm3: Abnormal renal function-NAC + non hydration Arm4: Abnormal renal function-saline 0.45% + NAC	Cr ≥ 0.5 mg/dl Time point: 48 hours Normal renal function Arm1: 23/330 (6.97) Arm2: 22/330 (6.67) P>0.05 Abnormal renal function Arm3: 64/188 (34.04) Arm4: 40/188 (21.28) P<0.01 All arms p<0.001							

Evidence Table U. Summary of the outcomes of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)*	Mortality n/N (%)	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days	Cardiac events, n/N (%)
Cho, 2010[14]	Arm1: IV Normal saline Arm2: IV NaHCO3 + IV Normal saline Arm3: Oral Normal saline Arm4: Oral Normal saline + Oral NAHCO3	Cr ≥25% or ≥0.5mg/dl Arm1: 6/27 (22.2) Arm2: 2/21 (9.5) Arm3: 1/22 (4.5) Arm4: 1/21 (4.7) Arm1 vs. Arm2 P=0.78 Arm1 vs. Arm3 P=0.62 Arm1 vs. Arm4 P=0.34 Arm2 vs. Arm3 P=0.84 Arm2 vs. Arm4 P=0.53 Arm3 vs. Arm4 P=0.66						Mean length of stay N (SD) Arm1: 4.2 (4.5 Arm2: 4.1 (4.0) Arm3: 4.4 (6.5) Arm4; 6.9 (9.4) P=0.66	

Evidence Table U. Summary of the outcomes of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)*	Mortality n/N (%)	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days	Cardiac events, n/N (%)
Koc, 2012[30]	Arm1: standard-dose IV Normal saline Arm2: IV NAC plus high-dose IV Normal saline Arm3: high-dose IV Normal saline	Cr ≥25% Arm1: 6 (10.0) Arm2: 2 (2.5) Arm3: 13 (16.3) P=0.012	Age >70 Arm1: 3 (14.3) Arm2: 0 (0) Arm3: 6 (18.9) P=0.14 LVEF <40 Arm1: 2 (15.0) Arm2: 1 (3.6) Arm3: 1 (5.6) P=0.50 Contrast dose >100ml Arm1: 4 (9.1) Arm2: 2 (4.2) Arm3: 9 (18.0) P=0.07 Diabetes Arm1: 3 (12.5) Arm2: 2 (6.7) Arm3: 3 (14.3) P=0.63 Baseline CrCl<50 Arm1: 3 (30.0) Arm2: 1 (4.8) Arm3: 8 (33.3) P=0.03			Change in Cr Arm1: 0 Arm2: -0.05 Arm3: 0 P=0.004	Age >70 Arm1: 0.1 (0.-0.20) Arm2: 0 (-0.20-0.10) Arm3: 0 (-0.10-0.20) P=0.08 LVEF <40 Arm1: 0.10 (0-0.20) Arm2: -0.05 (-0.20-0.10) Arm3: 0 (-0.10-0.1) P=0.037 Contrast dose >100ml Arm1: 0 (0-0.10) Arm2: 0 (-0.20-0.10) Arm3: 0 (-0.10-0.20) P=0.07 Diabetes Arm1: 0 (-0.10-0.18) Arm2: -0.005 (-0.20-0.20) Arm3: 0 (-0.25-0.15) P=0.30 Baseline CrCl Arm1: 0.15 (-0.03-1.8)Arm2: 0.10 (-0.15-0.20) Arm3: 0.05 (0.30-0.63) P=0.032		

Evidence Table U. Summary of the outcomes of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)*	Mortality n/N (%)	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days	Cardiac events, n/N (%)
Kong, 2012 [31]	Arm1: IV Normal saline Arm2: pre and post oral hydration Arm3: post oral hydration	Cr ≥25% Arm1: 2 (5) Arm2: 3 (7.5) Arm3: 2 (5) P=0.86	NR	Arm1: 0/40 Arm2: 0/40 Arm3: 0/40	NR	NR	NR	NR	NR
Krasuski, 2003 [33]	Arm1: overnight hydration 5% dextrose + 0.45% saline Arm2: IV Normal saline	Cr >0.5mg/dl 48 hours Arm1: 0 (0) Arm2: 4 (11) All arms P=0.136	CrCl <50ml/min 48 hours Arm1: 0/17 Arm2: 3/20 (15) All arms P=0.234	NR	Permanent dialysis 48 hours Arm1: 0/26 (0) Arm2: 2 (5.4)	NR	NR	NR	NR
Lawlor, 2007 [34]	Arm1: IV Normal saline + placebo Arm2: IV Normal saline + NAC Arm3: oral hydration + NAC	Cr ≥25% Arm1: 2 (8.0) Arm2: 2 (8.0) Arm3: 2 (7.0) P=0.99	Baseline Cr >200 µmol/L Arm1: 2(40.0) Arm2: 1(20.0) Arm3: 2 (33.0) P=0.78			Mean change in Cr N (SD), 48 hours Arm1: 173 (64) Arm2: 180 (61) Arm3: 173 (56) P=0.88	Baseline Cr >200 µmol/L Arm1: 267 (90) Arm2: 272 (62) Arm3: 250 (67)		

Evidence Table U. Summary of the outcomes of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)*	Mortality n/N (%)	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days	Cardiac events, n/N (%)
Maioli, 2011[39]	Arm1: no hydration Arm2: late Normal saline Arm3: early Normal salinesodium bicarbonate	Cr ≥25% Arm1: 41/150 (27.3) Arm2: 34/150 (22.7) Arm3: 18/150 (12.0) P=0.001	Cr ≥ 25% High to very high CIN risk >11 Arm1: 18/52(34.6) Arm2: 14/46(46) Arm3: 11/45(24.4) P=0.28 eGFR <60 Arm1: 10/34 (29.4) Arm2: 12/46 (26.1) Arm3: 6/45 (15.0) P=0.14 Age >75 years Arm1: 11/29 (37.9) Arm2: 15/36 (41.7) Arm3: 8/38 (21.1) P=0.12 Diabetes Arm1: 10/34 (29.4) Arm2: 11/31 (35.5) Arm3: 5/31 (16.1) P=0.24	Arm1: 8/150 (5.3) Arm2: 5/150 (3.3) Arm3: 3/150 (2.0) P=0.12	Arm1: 1/150 (0.7) Arm2: 1/150 (0.7) Arm3: 2/150 (1.3) P=0.54				Cardiogenic shock Arm1: 8/150 (5.3) Arm2: 9/150 (6.0) Arm3: 6/150 (4.0) P=0.6 Recurrent MI Arm1: 5/150 (3.3) Arm2: 6/150 (4.40) Arm3: 2/150 (1.3) P=0.30 Repeated urgent PCI Arm1: 2/150 (1.3) Arm2: 5/150 (3.3) Arm3: 1/150 (0.7) P=0.66 Stroke Arm1: 2/150 (1.3) Arm2: 2/150 (1.3) Arm3: 1/150 (1.3) P=1.0 MACE Arm1: 15/150 (10) Arm2: 19/150 (12.7) Arm3: 11/150 (7.3) P=0.44

Evidence Table U. Summary of the outcomes of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)*	Mortality n/N (%)	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days	Cardiac events, n/N (%)
Maioli, 2011[39] (continued)			Anterior MI Arm1: 22/65 (33.8) Arm2: 16/63 (25.4) Arm3: 1261 (19.7) P=0.07 LVEF <40% Arm1: 24/61 (39.3) Arm2: 20/58 (34.5) Arm3: 12/56 (21.4) P=0.04 Volume contrast to eGFR ratio >3.7 Arm1: 15/50 (30.0) Arm2: 15/55 (27.3) Arm3: 9/48 (18.8) P=0.20						
Marron, 2007[42]	Arm1: Normal saline Arm2: Hypotonic 0.45% saline	Cr ≥ 25% 24 hours Arm1: 5/37 (13.5) Arm2: 4/34 (11.7) P=NS 48 hours Arm1: 3/37 (8.1) Arm2: 1/34 (2.9) P=NS				Change in peak Cr 24 hours Arm1: -0.046 (0.004) Arm2: -0.079 (0.001) 48 hours Arm1: -0.008 (0.001) Arm2: -0.007 (0.003) All comparison NS			

Evidence Table U. Summary of the outcomes of studies comparing fluid strategies for the prevention of contrast-induced nephropathy and other outcomes (continued)

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)*	Mortality n/N (%)	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, mean (SD)	Length of hospital stay, mean days	Cardiac events, n/N (%)
Mueller, 2002[43]	Arm1: Normal saline Arm2: .45% NaCl + 5% glucose	Cr >0.5mg/dl 48 hours Arm1: 0/26 Arm2: 4/37 (11) All arms P=0.04	Cr >0.5mg/dl 48 hours Men Arm1: 4/507 (.8) Arm2: 5/522 (1) All arms P=0.77 Women Time point: 48 hours Arm1: 1/178 (.6) Arm2: 9/176 (5.1) All arms P=0.01 Diabetes Time point: 48 hours Arm1: 0/107 Arm2: 6/110 (5.5) All arms P=0.01 No diabetes Time point: 48 hours Arm1: 5/578 (.9) Arm2: 8/588 (1.4) All arms P=0.42	NR	NR	NR	Diabetes Arm1: .92 Arm2: .98 All arms P=0.13 No diabetes Arm1: .92 Arm2: .98 All arms P=0.13 Women Arm1: .81 Arm2: .84 All arms P=0.37 ≥250ml of contrast Arm1: 0.9 Arm2: 0.93 All arms P=0.25	Arm1: 4.8 Arm2: 4.8 All arms P=0.87	Major adverse cardiac event 30 days Arm1: 14 (5.3) Arm2: 17 (6.4) All arms P=0.59
Trivedi, 2003[56]	Arm1: oral hydration Arm2: IV Normal saline	Cr >0.5mg/dl 48 hours Arm1: 9 (34.6) Arm2: 1 (3.7) All arms P=0.005	NR	NR	Arm1: 20 (21) Arm2: 8 (11)	µmol/L 24 hours Arm1: 20 (21) Arm2: 8 (11); P=002 48 hours Arm1: 29 (40) Arm2: 12 (21) P=0.17	NR	NR	NR

CIN=contrast induced nephropathy; CrCl=creatinine clearance; eGFR=estimated glomular filtration rate; IV=intravenous; LVEF=left ventricular ejection fraction; MACE=major adverse cardiac events; MI=myocardial infarction; NR=not reported; PCI=percutaneous coronary intervention; Cr=creatinine; RRT=renal replacement therapy; SD=standard deviation

* n/N refers to number of events divided by number at risk.

Evidence Table V. Adverse events in studies comparing fluid strategies for the prevention of contrast induced nephropathy and other outcomes.

Author, Year	Adverse events
Bader,2004[7]	NR
Mueller, 2002[43]	Vascular complications, 13 cases in the control group and 12 cases in the treatment group
Chen, 2008[13]	Adverse events reported by CIN, non-CIN status; Many conditions listed have no known correlation with intervention. They include major bleeding, death secondary to stroke, mechanical ventilation, continuous veno-venous filtration
Cho, 2010[14]	Other: in-house mortality; 0 in all arms
Koc, 2012[30]	No adverse reactions besides CIN
Kong, 2012[31]	NR
Krasuski, 2003[33]	NR
Lawlor, 2007[34]	Other: adverse side effects to NAC or placebo; no adverse side effects related to treatment with NAC or placebo were reported; Acute renal failure; No patients developed acute renal failure that required dialysis following their angiograms
Maioli, 2011[39]	Other: Major bleeding, Arm1: 8 (5.3%), Arm2: 12 (8%), Arm3: 6 (4%), Stroke, 2 cases (1.3%) in each arm,
Marron, 2007[42]	NR
Trivedi, 2003[56]	Other: adverse effects of saline hydration, (Amongst patients with contrast-induced renal failure, hospitalization was prolonged in 3 patients in the control group and 1 patient in the treatment group)

CIN=contrast induced nephropathy; g/kg/day=gram per kilogram per day; NAC=N-acetylcysteine; NaCl=sodium chloride; NR=not reported

Evidence Table W. Summary of characteristics of studies comparing dopamine versus other interventions for the prevention of contrast-induced nephropathy and other outcomes

Author, year	Comparison	N	Population included	Age, range of means[§]	No. female (%)[‡]	Mean followup	CM Route	Definition of CIN*	Study limitations
Abizaid, 1999 [1]	0.45% saline vs. dopamine + 0.45% saline vs. aminophylline + 0.45% saline	60	Cr ≥1.5 mg/dl	74-75	20 (33)	6 days	LOCM (loxaglate) IA	A1	M
Hans, 1998 [22]	Placebo + Normal saline vs. Dopamine + Normal saline	55	Cr ≥1.4 mg/dL	71-75	6 (10)	4 days	LOCM (Iohexol) IA	A2	H

%=percent; CIN=contrast induced nephropathy; CM=contrast media; HOCM=high-osmolarity contrast media; IA=intrarterial; IVF=intravenous fluid; LOCM=low osmolarity contrast media; Mg/dl=milligram per deciliter; Mg/kg/hour=milligram per kilogram per hour; N=sample size; Ug/kg/min=microgram per kilogram per minute; vs.=versus; Cr=creatinine

* CIN definitions: rise in serum creatinine relative to baseline: ≥25% (A1); ≥0.5 mg/dl (A2); ≥25% or ≥0.5 mg/dl (A3); ≥50% (A4), B: >25% reduction in creatinine clearance
† Study limitations: L=low risk of bias; M=moderate risk of bias; H=high risk of bias
‡ Percent females in entire study population
§ Some studies only reported mean age per arm, not one mean for whole population. This column shows range of the means across all arms.

Evidence Table X. Summary of the outcomes of studies comparing dopamine versus other interventions for the prevention of contrast-induced nephropathy

Author, year	Comparison	Incidence of CIN, n/N (%)	Incidence of CIN: subgroups, n/N (%)*	Mortality, n/N (%)	Need for RRT, n/N (%)	Change in Cr, mean (SD)	Change in Cr: subgroups, Mean (SD)	Length of hospital stay, mean days	Cardiac events, n/N (%)
Abizaid, 1999 [1]	Arm1: 0.45% IV Normal saline Arm2: dopamine + 0.45% saline Arm3: aminophylline + 0.45% saline	Cr ≥25% Time point: NR Arm1: 6/20 (30) Arm2: 10/20 (50) Arm3: 7/20 (35); P=0.60	NR	NR	Time point: NR Arm1: 0/20 (0) Arm2: 0/20 (0) Arm3: 1/20 (5); P=1.00	At 48 hours Arm1: 0.5 (0.2) Arm2: 0.6 (0.2) Arm3 0.4 (0.3); P=0.06	NR	Arm1: 7.0 Arm2: 6.8 Arm3: 7.0; P=0.82	NR
Hans, 1998 [22]	Arm1: placebo + Normal saline Arm2: dopamine + Normal saline	Cr ≥0.5 mg/dl At 24 hours Arm1: 7/27 (25.9) Arm2: 0/28 (0); P=0.002 At 48 hours Arm1: 8/27 (28.6) Arm2: 2/28 (7.1); P=0.026 At 72 hours Arm1: 10/27 (27.0) Arm2: 4/28 (14.3); P=0.048 At 96 hours Arm1: 12/27 (44.4) Arm2: 5/28 (17.9); P=0.031	NR	NR	NR	At 24 hours Arm1: 0.193 (0.287) Arm2: -0.018 (0.172); P=0.002 At 48 hours Arm1: 0.211 (0.339) Arm2: 0.089 (0.218); P=0.118 At 72 hours Arm1: 0.330 (0.626) Arm2: 0.114 (0.351); P=0.120 At 96 hours Arm1: 0.333 (0.626) Arm2: 0.132 (0.309); P=0.134	Subgroup: Cr ≥2 mg/dL At 24 hours Arm1: 0.803 (0.361) Arm2: 0.018 (0.098); P=0.031 At 48 hours Arm1: 0.444 (0.401) Arm2: 0 (0.126); P=0.012 At 72 hours Arm1: 0.789 (0.896) Arm2: 0.064 (0.280); P=0.044 At 96 hours Arm1: 0.733 (0.890) Arm2: 0.038 (0.229); P=0.049	NR	NR

ANP=Atrial natriuretic peptide; CIN=contrast induced nephropathy; Cr=creatinine; IABP=intra-aortic balloon pump; IV=intravenous; NR=not reported; RRT=renal replacement therapy; VT/VF= Ventricular fibrillation and or ventricular tachycardia

* n/N refers to number of events divided by number at risk.

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